BioElectronics

Physics & Clinical Evidence of Pulsed Shortwave Frequency Therapy

For the Reduction of Pain, Inflammation and Accelerated Healing

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THE WALL STREET JOURNAL.

BioElectronics Corporation pulsed radio frequency electromagnetic field therapy, is changing the way people heal. BioElectronics has taken an old established technology delivered by large expensive machines and made it accessible for all. By reducing the size, to a lightweight wearable device, and extending the time of the therapy, patients can go about their daily lives receiving therapy every minute of the day. Clinical studies, some published in the 1960's showed that the energy of RF electromagnetic field had great therapeutic value. Patients had significantly improved pain, faster healing times and improved function. Challenging chronic wounds were also shown to be effectively treated. The major obstacle to the wide use of this therapy has not been the clinical effectiveness, or the safety. In fact, in all the published clinical studies there were no reports of detrimental side effects, in fact no side effects at all. The size of the devices and cost has been the reason that this therapy is not widely employed in clinical practice. For example, healing of wounds requires two 30 minute treatments per day, effectively limiting its use to the most severe cases. Now all that has changed, with peer reviewed clinical studies published in established medical journals, it's now becoming clearer than ever that BioElectronics devices have the same therapeutic efficacy of reducing pain and promoting healing as the established large clinical devices. The significance difference is that Bioelectronics devices are economical, simple to use, easy to wear and portable.

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BioElectronics Corporation

Pulse Radio Frequency Electromagnetic Energy

Energy for Healing

Wound healing is a complex process that involves inflammation, cell proliferation, formation of granulation tissue, production of new structures and tissue remodeling. Healing of all tissue injury involves these phases of healing, and normally results in scar tissue formation.

Pulsed radio frequency electromagnetic energy, through decades of research has been shown to significantly shorten each phase of the wound healing process. By reducing the inflammation phase, increasing cell proliferation and activity leading to the combined and coordinated effects of wound contracture and granulation tissue maturation associated with collagen deposition, with the end result reflected in an accelerated healing response.

PHASES OF HEALING
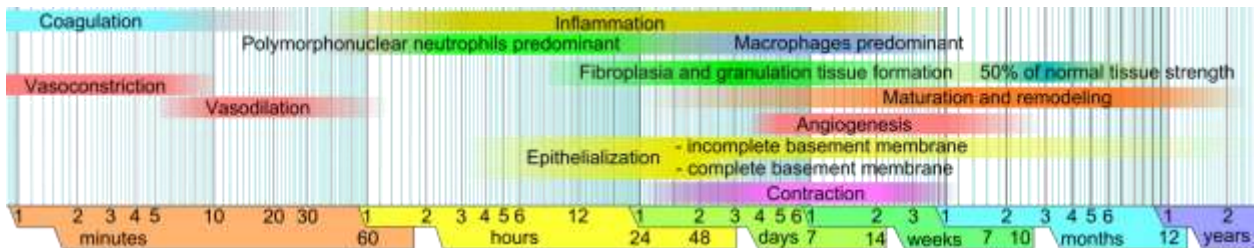
Introduction

MEDICAL APPLICATIONS - SHORTWAVE RADIO FREQUENCY

Therapeutic medical application of radio frequency (RF) energy at a carrier frequency between 13–27.12MHz is referred to as shortwave diathermy and can be divided into two general categories based on mode of delivery: continuous RF energy delivery and pulsed RF energy delivery. Continuous delivery of shortwave energy to a tissue leads to an increase in tissue temperature, and is used for the therapeutic delivery of deep heat. Delivery of pulsed RF energy to a tissue can allow for the dissipation of heat between pulses, providing therapeutic effects in the absence of substantial tissue temperature elevation, a therapy first developed to diminish negative complications that can occur with tissue heating, while conserving other therapeutic benefits of this type of application. While tissue heating with pulsed RF energy is deemed to be insignificant, new research suggests that there is a thermal component to pulsed RF energy which may offer significant therapeutic effects on soft tissues. Pulsed RF energy has a wide range of therapeutic uses, is well tolerated due to the non-invasive nature of application, and serves as an effective adjunctive treatment for many conditions. Non thermal therapeutic uses of pulsed radio frequency are currently being used to treat pain and edema, chronic wounds, and bone repair.

Pulsed radio frequency electromagnetic field therapy (PRFE), or pulsed electromagnetic field (PEMF) therapy has a long history in treating medical conditions. In 1947 the Federal Communications Commission assigned three frequencies at the short end of the RF band for medical use (40.68 MHz, 13.56 MHz and 27.12 MHz). The frequency of 27.12 MHz is the most widely used in clinical practice. The first PRFE device, the Diapulse (Diapulse Corporation, NY) was commercially available in the 1950's, and was followed by other commercially available machines. PRFE is a non-invasive therapy that delivers electromagnetic energy into soft tissue generating an electric field which is thought to mediate the therapeutic effects. BioElectronics Corporation range of pulsed radio frequency electromagnetic energy devices operate in the shortwave form of 27.12Mhz.

A Thermal Component of Pulsed Radio Frequency Energy Therapy?

The peripheral neural system is now known to be highly temperature sensitive, and many other specific sites and mechanisms of thermal sensitivity have been identified. Temperature increases in tissues as low as 0.1°C have significant biological affects which include:
- Vasodilation
- ↑rate of cell metabolism
- ↑ capillary permeability
- ↑delivery of leukocytes
- Removal of metabolic waste
- ↑ elasticity of ligaments, capsules, and muscle
- Analgesia and sedation of nerves

- ↑nerve conduction
- ↓muscle tone
- ↓ muscle spasm

We gratefully acknowledge that the following section is the work of Professor Tim Watson (Professor Tim Watson, School of Health & Emergency Professions, University of Hertfordshire, UK) and can found at www.electrotherapy.org*.*

The early development of RF energy application was termed diathermy, which literally means heating through. Termed, because unlike externally applied heat the RF energy is able to penetrate relatively deep into soft tissue resulting in a deep heating effect. Pulsing was introduced to eliminate these heating effects and reduce the adverse effects of heat induced tissue damage. However, pulsing the RF energy has proven to eliminate thermal damage a thermal therapeutic effect cannot be ruled out. Recent research suggests that a thermal component of pulsed RF energy may still be a factor in the therapeutic effects of PRFE. With respect to the effects of pulsed shortwave diathermy, there is an element of tissue heating which occurs during the `on' pulse, but this is dissipated during the prolonged 'off' phase. Clearly during the delivery of each pulse there will be a (very small) thermal change and the potential thermal effect of pulsed short wave is dependent on 3 parameters:

Pulse Repetition Rate (Hz or pps)
the number of pulses delivered per second
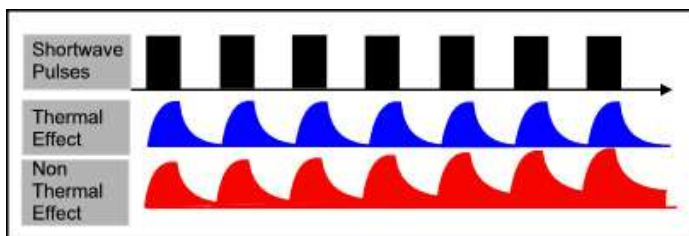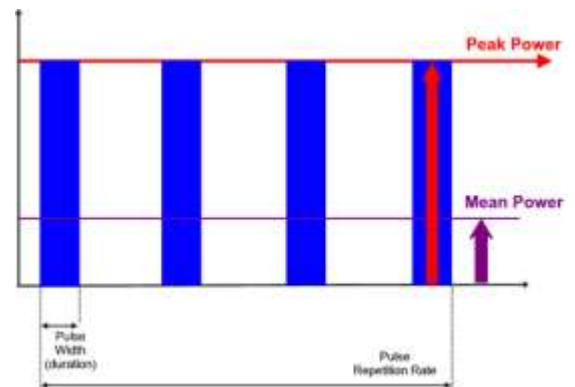**Pulse Duration (Width) (microseconds)**
the duration (time) of each 'ON' phase
Power (Peak and Mean)
power delivered from the device (during pulse - PEAK and averaged over time to - MEAN)

In this example the pulse rate is sufficiently spaced so that there is no thermal build up.
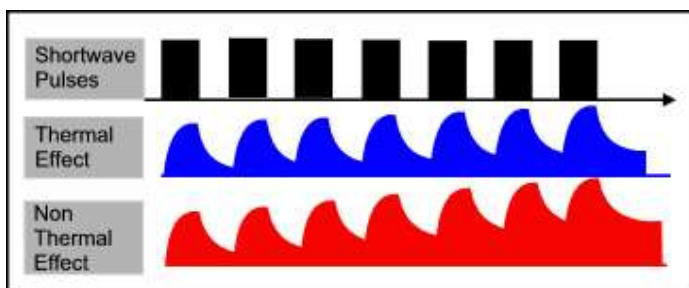
In this example a high pulse rate results in a non-thermal and thermal build up.

The externally applied continuous application of low level heat has recently shown to be therapeutically effective in a series of clinical studies. However, externally applied low level heat results in minimal deep tissue heating. Pulsed RF as a continuous application is able to apply physiologically significant levels of heat deep into the target tissue, without corresponding negative effects of thermally induced tissue damage. The dual thermal and electrical therapy of pulsed RF electromagnetic energy provides a unique dynamic approach to pain reduction and the acceleration of healing.

Non-Thermal Mechanism of Action of Pulsed Radio Frequency Electromagnetic fields

The mechanism of action of Pulsed Radio Frequency Electromagnetic Field (PRFE) on wound healing and control of pain is beginning to be understood based on a number of cell and animal studies. The mechanism of Ca^{2+} calmodulin signaling leading to nitric oxide (NO) production is covered by a review article Strauch et al 2009 and a figure from the article is presented below(Strauch, Herman et al. 2009).
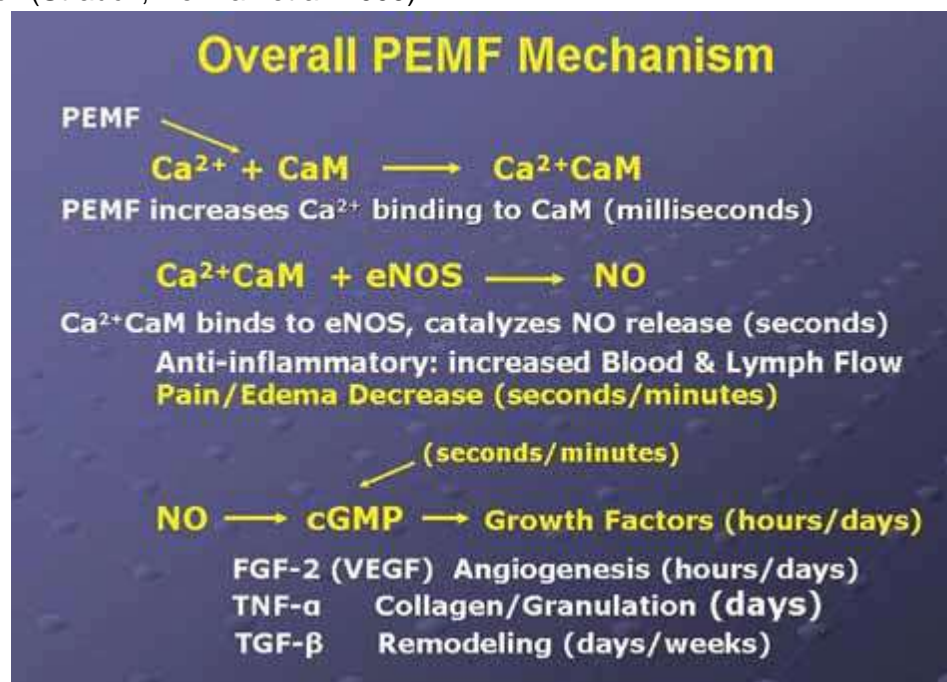
Figure 1. A proposed model for Pulsed electromagnetic field (PEMF) transduction mechanism based on evidence to date that many athermal PEMF effects depend upon nitric oxide cascades. PEMFs can be configured to modulate calcium-binding kinetics to calmodulin. Calcium/calmodulin then activates nitric oxide synthase and the relevant cascade ensues dependent upon stage of tissue repair process. This mechanism has been proposed as a working model for PEMF therapeutics.

A number of cellular studies show PRFE has effects on production of nitric oxide(Diniz, Soejima et al. 2002; Kim, Shin et al. 2002; Fitzsimmons, Gordon et al. 2008; Yue, Yang et al. 2008; Lee, Kwon et al. 2010), increased cell proliferation(Diniz, Soejima et al. 2002; Kim, Shin et al. 2002; Fitzsimmons, Gordon et al. 2008; Yue, Yang et al. 2008; Lee, Kwon et al. 2010), and in vivo vasodilation in rat muscle(Smith, Wong-Gibbons et al. 2004). It is known that NO is a critical molecular signal and mediator for normal wound healing(Boykin 2010; Filippin, Cuevas et al. 2011), and NO deficiency has been established as an important mechanism responsible for poor healing in diabetic foot ulcer patients(Filippin, Cuevas et al. 2011).

Co-cultures of human dermal fibroblasts and human epidermal keratinocytes exposed to PRFE demonstrated an up-regulation of gene families involved in tissue repair. These include matrix metalloproteinase (MMP,s) and tissue inhibitor of metalloproteinase (TIMP's), and cytokines - interleukin (IL)-related genes, interferon (INF)-related genes, and tumor necrosis factor (TNF)-related genes (attached).
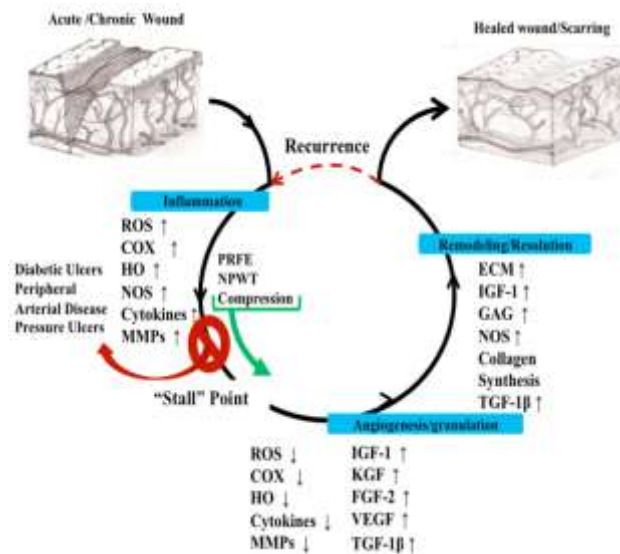
The growth factor, fibroblast growth factor-2 (FGF-2) has also been shown to be up-regulated by PRFE treatment. FGF-2 promotes endothelial cell proliferation and the physical organization of endothelial cells into tube-like structures, thus promoting angiogenesis. As well as stimulating blood vessel growth, FGF-2 is important player in wound healing, stimulating proliferation of fibroblasts and endothelial cells that give rise to angiogenesis, and developing granulation tissue as well as increasing blood supply. A number of animal and cell studies have demonstrated FGF-2 up-regulation after PRFE treatment. In a mouse model of diabetes, PRFE treatment improved healing with the up-regulation of FGF-2 and was able to prevent tissue necrosis in diabetic tissue after an ischemic insult (Callaghan, Chang et al. 2008). Angiogenesis mediated by FGF-2 up-regulation as well as angiopoietin-2 was reported in bones of mice treated with PRFE (Goto, Fujioka et al. 2010). A study on endothelail cells treated with PRFE also demonstrated a FGF-2 up-regulation and increased endothelial tubular formation with the effects mitigated by FGF-2 neutralizing antibody (Tepper, Callaghan et al. 2004).

Though not significant, FGF-2 was shown to be up-regulated in wounds after breast reduction surgery (Rohde, Chiang et al. 2010). Taken together these studies indicate that PRFE therapy can up-regulate mechanisms involved in tissue repair including growth factors and cytokines important for the wound healing process.

The medical applications of PRFE therapy has recently been well reviewed by Guo et al(Guo, Kubat et al. 2011).

References

Boykin, J. V., Jr. (2010). "Wound nitric oxide bioactivity: a promising diagnostic indicator for diabetic foot ulcer management." J Wound Ostomy Continence Nurs **37**(1): 25-32; quiz 33-24.

Callaghan, M. J., E. I. Chang, et al. (2008). "Pulsed electromagnetic fields accelerate normal and diabetic wound healing by increasing endogenous FGF-2 release." Plast Reconstr Surg **121**(1): 130-141.

Diniz, P., K. Soejima, et al. (2002). "Nitric oxide mediates the effects of pulsed electromagnetic field stimulation on the osteoblast proliferation and differentiation." Nitric Oxide **7**(1): 18-23.

Filippin, L. I., M. J. Cuevas, et al. (2011). "Nitric oxide regulates the repair of injured skeletal muscle." Nitric Oxide **24**(1): 43-49.

Fitzsimmons, R. J., S. L. Gordon, et al. (2008). "A pulsing electric field (PEF) increases human chondrocyte proliferation through a transduction pathway involving nitric oxide signaling." J Orthop Res **26**(6): 854-859.

Goto, T., M. Fujioka, et al. (2010). "Noninvasive up-regulation of angiopoietin-2 and fibroblast growth factor-2 in bone marrow by pulsed electromagnetic field therapy." J Orthop Sci **15**(5): 661-665.

Guo, L., N. J. Kubat, et al. (2011). "Pulsed radio frequency energy (PRFE) use in human medical applications." Electromagnetic biology and medicine **30**(1): 21-45.

Kim, S. S., H. J. Shin, et al. (2002). "Enhanced expression of neuronal nitric oxide synthase and phospholipase C-gamma1 in regenerating murine neuronal cells by pulsed electromagnetic field." Exp Mol Med **34**(1): 53-59.

Lee, H. M., U. H. Kwon, et al. (2010). "Pulsed electromagnetic field stimulates cellular proliferation in human intervertebral disc cells." Yonsei Med J **51**(6): 954-959.

Nicolle, F. V. and R. M. Bentall (1982). "Use of radio-frequency pulsed energy in the control of postoperative reaction in blepharoplasty." Aesthetic Plast Surg **6**(3): 169-171.

Rawe, I. M. and T. C. Vlahovic (2011). "The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: A case report." Int Wound J.

Rohde, C., A. Chiang, et al. (2010). "Effects of pulsed electromagnetic fields on interleukin-1 beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients." Plast Reconstr Surg **125**(6): 1620-1629.

Smith, T. L., D. Wong-Gibbons, et al. (2004). "Microcirculatory effects of pulsed electromagnetic fields." J Orthop Res **22**(1): 80-84.

Strauch, B., C. Herman, et al. (2009). "Evidence-based use of pulsed electromagnetic field therapy in clinical plastic surgery." Aesthet Surg J **29**(2): 135-143.

Tepper, O. M., M. J. Callaghan, et al. (2004). "Electromagnetic fields increase in vitro and in vivo angiogenesis through endothelial release of FGF-2." FASEB J **18**(11): 1231-1233.

Yue, A., G. Yang, et al. (2008). "[The influence of the pulsed electrical stimulation on the morphology and the functions of the endothelial cells]." Sheng Wu Yi Xue Gong Cheng Xue Za Zhi **25**(3): 694-698.

Electric Fields and the Enhancement of wound healing

Pulsed radio frequency electromagnetic fields result in two basic fields: the electric field and magnetic fields that are generated in the soft tissue. It is these fields and the currents generated in the soft tissue that are thought to cause the heat for the thermal component and the currents that can exert changes in cellular activity. In has been known for many years that endogenous DC electric fields are important, fundamental components of development, regeneration, and wound healing. The fields are the result of polarized ion transport and current flow through electrically conductive pathways. Blocking of endogenous electric fields with pharmacological agents or applied electric fields of opposite polarity disturbs the aforementioned processes, while enhancement increases the rate of wound closure and the extent of regeneration. Electric fields are applied to humans in the clinic, to provide an overwhelming signal for the enhancement of healing of chronic wounds. Although clinical trials, spanning a course of decades, have shown that applied electric fields enhance healing of chronic wounds, the mechanisms by which cells sense and respond to these weak cues remains unknown. Electric fields are thought to influence many different processes *in vivo*. However, under more rigorously controlled conditions *in vitro*, applied electric fields induce cellular polarity and direct migration and outgrowth.
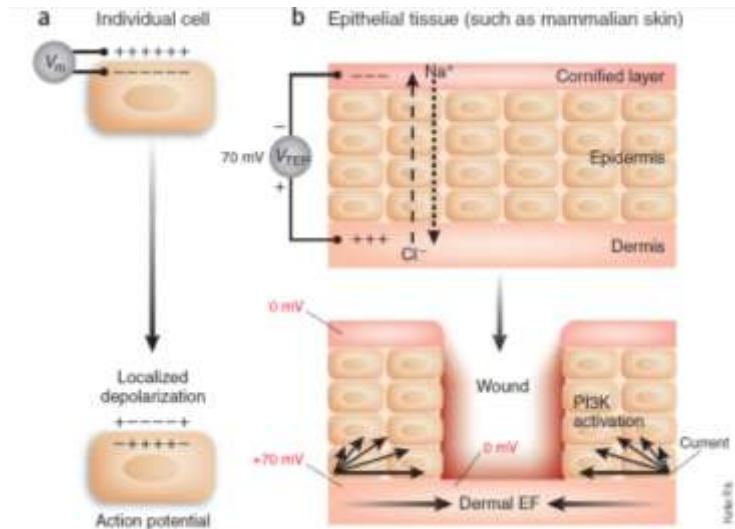
Action potential in individual cells and injury potential in tissues. (**a**) Individual cells maintain an electrical potential across the plasma membrane (*V*m) as a result of the activity of membrane-bound ion channels. This results in a net negative charge on the inside of the cell relative to the outside. This resting membrane potential can be locally depolarized under the influence of cell stimuli, leading to an inward current (bottom). (**b**) Schematic representation of the generation of a transepithelial potential (*V*TEP) in human skin (individual cells in cornified layer and dermis are not shown). Selective, directional ion transport across the intact epithelium gives rise to a *V*TEP that can be measured directly across the epithelium (top; 70 mV in this case). Tight junctions between epithelial cells (not shown) create physical connections between cells, providing high electrical resistance to the epithelial sheet. Wounding of an epithelial sheet results in collapse of the *V*TEP at the wound (to 0 mV) without affecting the *V*TEP distally (70 mV). Na+ leaks out of the wound, resulting in an injury current toward the cut (thin arrows) and a lateral voltage gradient oriented parallel to the epithelial sheet (EF, electric field; thick arrows at bottom). The wound site is the cathode of the electric field (bottom). [Bart Vanhaesebroeck 2006 Charging the batteries to heal wounds through PI3K. Nature Chem Biol. 2:9]

Pulsed Radio Frequency Device Innovation

The first PRFE device to be commercially developed in the 1950's was the Diapulse. These were large bulky clinic based PRFE devices as shown in figure 1A. Treatment regimens often consist of daily multiple 20 or 30 minutes treatments. Modern PRFE devices are smaller and more portable figure 1B, but still require mains power and still require daily treatment regimens. Despite the large number of clinical studies showing significant therapeutic effects (appendix table), the daily treatment regimens are a major handicap to the wide adoption of PRFE therapy as a postoperative treatment, injury recovery and an adjunct therapy for wound healing. Another obstacle to their wide adoption is the initial purchase costs which can range into thousands of dollars restricting home based use. Innovative research in the 1970's and 1980's by Dr. Bentall began to demonstrate that mains powered PRFE devices delivering relatively high energy treatments for short periods, could be replaced by extended time low energy treatments by portable wearable battery powered devices. This initial innovation and discovery led to the development of Bioelectronics range of wearable extended use PRFE devices with an example shown in figure 1C.

Figure 1. Shows a (A) Diapulse, (B) Provant Therapy System and (C) BioElectronics RecoveryRx, each device utilizes a 27.12MHz carrier frequency.

A. Diapulse	B. Provant Therapy System	C. BioElectronics RecoveryRx
A fixed clinic based PRFE device with a daily 2 x 30 min treatment regime	Suit case sized device offering portability with treatment regimens of 2x 30 min daily	Wearable PRFE device weighing 8g which operates for 1 week of continuous therapy

Extended treatment time Pulsed Radio Frequency Studies

The development of the Bioelectronics device was based on a pioneering work by Dr. Bentall. At the Proceeding of the 1st annual meeting of the Bioelectrical Repair and Growth Society. Dr. Bentall presented data comparing the effects of a 15 Watt pulsed radio frequency device at 27.12 MHz (Diapulse) to a 2 milliwatt pulsed device at 3 MHz on the tensile strength of rat abdominal wounds. Despite the large difference in the physical size and power output of the two devices, they showed a very similar profile in enhancing the tensile strength of the wounds. The 15 watt Diapulse treatment was given 3 x 20 min per day and the 2 milliwatt treatment was an overnight exposure, control was a 15 Watt light bulb. This was the first study to show that lower power with longer treatment duration was as effective as higher power shorter treatments. In unpublished studies on human experimental wounds, Bentall looked at full-thickness skin wounds 3 mm diameter on 20 patient volunteers. Ten patients received continuous radio frequency treatment, with a device powered by a 3.5 volt battery with a carrier frequency of 44 MHz, 100□sec pulse width and pulse frequency of 1 KHz. The observations from this study were that treatment of skin wounds with continuous pulsed radio frequency accelerated healing, and improved the histological appearance of the wounds.

Nicolle & Bentall (1982) published a pilot study with 21 patients on the use of a proprietary pulsed radio frequency energy device on the control of postoperative edema and bruising after blepharoplasty surgery. The initial published pilot results showed promising results. A larger patient set was assessed involving 61 patients, with results showing after 3 days of continuous (16 hrs/day) treatment a clear reduction in bruising and edema in patients who received pulsed radio frequency therapy.

Dr. Bentall published the following publication highlighting a number of pioneering studies using extended use pulsed radio frequency fields.

R. H .C. BENTALL LOW-LEVEL PULSED RADIOFREQUENCY FIELDS AND THE TREATMENT OF SOFT-TISSUE INJURIES Bioelectrochemistry and Bioenergetics, 16 (1986) 531-548 A section of J. ElectroanaL Chem., and constituting Vol . 212 (1986)

Institute of Bioelectrical Research, Romanno Bridge, West Linton, Peeblesshire, EH46 7BY (Great Britain)
(Manuscript received April 19th 1986)

SUMMARY
The aim of this lecture is to outline the main physiological processes involved in the heating of wounds and to suggest a mechanism by which pulsed radiofrequency (RF) energy, or the currents induced in tissues by the application of that energy, may influence its course. Emphasis is given to the part played by oedema in inhibiting the processes of wound healing. Reference is made to the growing evidence that pulsed RF energy affects the time course of wound healing and the hypothesis is proposed that one possible mechanism by which pulsed RF energy accelerates wound healing is by reducing oedema.

INTRODUCTION
Interest in the therapeutic potential of pulsed RF energy was stimulated following reports of bioelectric fields being associated with amphibian limb regeneration and bone mechanics [1-3]. It was at about the same time the first reports of the use of pulsed electromagnetic fields in relation to wound healing emerged [4-10].

Much of the initial work, particularly in the orthopedic applications, was performed using direct current, pulsed direct current or alternating current, but more recently similar effect on bone healing have been demonstrated using pulsed electromagnetic field [11-13]. Watson [14] has reviewed bioelectrical effects in hard tissue applications and Frank and Szeto [15] have reviewed electromagnetically enhanced soft-tissue wound healing.

It was noted by Cameron [7] that pulsed radio frequency treatment of a surgical incision in the dog resulted in less severe oedema than in the untreated controls. If pulsed RF energy reduces oedema and so accelerates the preliminary stages of wound healing, it should also enhance the second and third phases. It is this hypothesis that has been investigated.

* Invited lecture delivered at the VIIIth International

Types of wound healing

Wound healing is usually divided into four main types according to the type of tissue involved and the nature and treatment of the wound [16] :
(i) Primary wound healing - a soft-tissue wound closed by surgical procedure. This occurs in the vast majority of surgical wounds in which the edges of the wound are apposed.
(ii) Secondary wound healing - a soft-tissue wound left to granulate as a means of closure. This occurs in wounds in which the edges are widely separated either as a deliberate surgical policy or as a consequence of tissue loss or destruction. This type of wound healing is most often encountered in pressure sores, leg ulcers and burn injuries.
(iii) Hard tissue healing - the repair of fractures by bone regeneration - this will not be covered further.
(iv) Healing in specialized tissues - lining epithelia and nerve tissue.

Phases of wound healing

The features of wound healing involve an acute inflammatory phase, a reparative phase, and a remodeling phase [17-20]. The time span for these events to take place can be measured in minutes and hours in the first phase, days to weeks in the second, and months to years for the third and final phase, at the end of which the wound is completely healed.

These three phases of wound healing consist principally of the following physiological events:

(a) The acute inflammatory reaction phase
(i) Changes in vascular permeability.
(ii) Appearance of fibrin.
(iii) Infiltration of leucocytes and macrophages.
(iv) Localized extravasation of blood.
(v) Alteration in histamine and local hormone levels associated with bradykinins, prostaglandins and complement .
(b) The reparative phase
(i) Decrease in local inflammatory reaction.
(ii) Appearance of fibroblasts in the wound area.
(iii) Associated production of collagen by the fibroblasts leading to increased wound tensile strength .
(iv) Absorption of extravagated blood constituents.
(v) Epithelial migration and basal cell mitotic activity.
(c) The remodeling phase
(i) Longer period of slower collagen deposition.
(ii) Crosslinking of collagen fibres.
(iii) Repair of nerve endings.
(iv) Formation of scar tissue.

In secondary wound healing the following additional events occur during the reparative phase:

(i) Proliferation of capillary loops into the defect.
(ii) Formation of granulation tissue in the area of tissue loss.
(iii) Epithelial migration over the granulation tissue.
(iv) Maturation of fibrous tissue from the granulation tissue.

A disadvantageous feature of secondary wound healing is that when the granulation tissue is resorbed it converts into massive fibrous tissue which leaves a puckered scar.

Factors affecting wound healing

There are many factors which influence the course of healing; the main factors of importance are listed below [18,21-25]:

(i) Blood flow to the site of injury.
(ii) Transport of oxygen to the wound.
(iii) Oedema and inflammatory reaction in the wound.
(iv) Nutritional status (Vitamin A, B, C and D, zinc and proteins are all essential).
(v) Underlying pathologies, e.g. renal failure, diabetes mellitus.
(vi) The effects of some drugs, e.g. steroids.

Wound healing and edema

Blood flow and hence the transport of oxygen to the wound is of paramount importance in the normal sequence of healing. Respiratory uptake of oxygen by hemoglobin in red blood cells occurs in alveoli in the lungs. It is then transported in the peripheral circulation to capillaries in

the tissues. Oxygen diffuses out of the capillaries, through the interstitial spaces and into the cells. The rate of diffusion depends upon the oxygen tension gradient across the interstitial space and the overall distance between the capillaries and the cells [22,26].

Oedema is an accumulation of fluid in the interstitial spaces between the cells [27]; it is the cause of swelling and, in the case of a surgical wound, may cause visible tension around the suture line [28]. Oedema occurs during the inflammatory reaction phase of wound healing as a result of changes in micro vascular permeability [29].

In Sevitt's classic work in 1958 [30] he described the cycle of events following bum injury which leads to tissue necrosis. He pointed out that oedema reduces the perfusion pressure by raising the pressure within the tissue. Oedema occludes the capillaries at the site of the wound and thereby prevents the flow of blood. This in turn reduces the supply of oxygen to the cells [31]. In addition, the accumulating oedema between the cells and the capillaries increases their physical separation which slows oxygen diffusion from the capillaries to the cells. This view is supported by the work of Remensnyder [32] demonstrating that steep oxygen gradients exist over very short distances surrounding a 1 mm burn of the rat cremaster. Moreover, he showed that the hypoxic areas of the wounds corresponded to the observable areas of vascular stagnation and thrombus formation.

The influence of oedema is not limited to the inflammatory phase of wound healing. For example, Speer [33], using a primary wound healing model, demonstrated a significantly lower tensile strength in the portion of a wound which had been associated with relatively severe oedema. He also documented evidence that the oedematous areas of the wound showed relatively slow afferent and efferent microcirculation compared with the non-oedematous areas. It seems likely that the dynamics of the microcirculation is altered by oedema. The destructive inflammatory phase of wound healing is thus prolonged, resulting in the delayed onset of the collagen synthesis phase of wound healing [34].

This concept of a prolonged inflammatory phase of wound healing is supported by the demonstration [29] that low tissue oxygen tension (indirectly caused by oedema) may be responsible for increased capillary permeability. The existing interstitial oedema is thus further compounded.

In conclusion, oedema exerts three detrimental effects during the inflammatory phase of wound healing:

(i) Stagnation due to increased tissue tension.
(ii) Increased distance for oxygen diffusion.
(iii) Increased permeability of the capillaries.

These effects interact to delay the onset of collagen production which, in turn, delay the development of tensile strength of the wound.

TENSILE STRENGTH OF RAT ABDOMINAL WOUNDS

Introduction
The effect of pulsed RF energy on the development of tensile strength of a wound was investigated in a laboratory animal model. The purpose of this study was to compare, at two time intervals following surgery (2 days and 8 days), the tensile strength of rat abdominal wounds treated with one of two pulsed radiofrequency devices (15 W or 2 mW nominal output) compared with a placebo
equivalent (15 W light bulb).

Method
110 Wistar rats (200 grams) were used in this study. Under ether anesthesia a 2.5 cm transverse incision was made in the abdominal wall through to the peritoneal cavity of each rat.

The wounds were closed with five interrupted silk sutures through all layers and the rats were randomly assigned to one of three treatment groups : 15 W, 2 mW or placebo.

The daily treatment regimen for each of the groups respectively was three episodes of 20 min exposures to the 15 W device, overnight exposure to the 2 mW device, or three episodes of 20 min exposure to the 15 W light bulb. Treatment continued until the randomized sacrifice of each animal at two or eight days
post-operatively.

Prior to sacrifice each rat was anaesthetized, a plastic bag was inserted into its peritoneal cavity and its sutures were removed. The bag was progressively inflated with water at a constant rate until the wound ruptured, The pressure of water in the bag was recorded continuously to determine the resistance of the wound to increasing intra-abdominal pressure
.

Device specifications
(i) Placebo device - 15 W light bulb.
(ii) 15 W pulsed RF device:
Nominal power output 15 W
Carrier frequency 27 MHz
Pulse width 65 µs
Pulse repetition frequency 200 Hz
(iii) 2 mW pulsed RF device:
Nominal power output 2 mW
Carrier frequency 3 MHz
Pulse width 100µs
Pulse repetition frequency 1 kHz

Results
The profiles of the tracings of pressure against time were different at the two different time intervals. Two days after incision the wounds were still quite weak and there was a single point at which each wound completely broke down. Eight days after incision there was a biphasic response. A first pressure peak was reached when the fascia ruptured, allowing the bag to spread out and the water pressure to drop. A second peak was then reached when the skin itself parted.
Three separate methods were used to quantify the tensile strength of the wounds:
(i) End volume - the total volume of water infused into the bag when the wound burst. This value was extremely variable at eight days and is not reported.
(ii) Area under the graph - this integrates the time period (seconds) over which pressure of water (mm Hg) was withstood and hence allows for different sized peritoneal cavities and for differences in the extent to which the bags spread out.
(iii) Wound index (8 day groups only) - this is the sum of the two pressure peaks multiplied by the time difference (in seconds) between them.

TABLE 1
Tensile strength of rat abdominal wounds at two and eight days following transverse surgical incision T tests were used to compare the experimental groups with the placebo groups and the results are shown in Table 1.

TABLE 1
Tensile strength of rat abdominal wounds at two and eight days following transverse surgical incision

	2 day			8 day		
	value	% increase	P value	value	% increase	P value
Placebo groups n=25						
End volume	97.7	-	-	-	-	-
Area under graph	1777.2	-	-	13116.4	-	-
Wound index	N/A	-	-	10563	-	-
15 W groups n=25						
End volume	112.7	15.4	0.025	-	-	-
Area under graph	2252.2	26.7	0.025	20642.5	57.4	0.025
Wound index	N/A	-	-	17563.4	66.3	0.025
2 mW groups n=5						
End volume	113.6	16.5	0.025	-	-	-
Area under graph	3256.6	83.2	0.01	13910.0	1.1	NS
Wound index	N/A	-	-	15287.0	44.7	0.01

Conclusions

These results clearly show that pulsed radiofrequency energy from both these devices does have a significant effect on the tensile strength of rat abdominal wounds. Despite the gross differences in the physical size and power output of the two devices (15 W and 2 mW), they showed a very similar profile of activity in enhancing the development of tensile strength. This confirms that the effect of pulsed radio frequency energy on wound healing is not thermal in origin.

HUMAN EXPERIMENTAL SKIN WOUNDS
Introduction

If an effect of pulsed RF energy on oedema leads to improved oxygen supply and the earlier appearances of the reparative events of the second phase of wound healing, its beneficial properties will not be confined to primary wound healing. Two double-blind experiments were performed to determine the effect of treatment with pulsed RF fields on the histological appearance of repaired human full-thickness punch wounds of the skin of the lower limbs. This is a secondary wound healing model which permits good experimental control. The first experiment sought to establish whether any effect of pulsed RF field could be observed.

The purpose of the second experiment was to investigate at what point in time the thickened epithelium observed in the first study developed, and to obtain histological evidence confirming that the events of the reparative phase of wound healing occur earlier in the treated wounds.

Method
Experiment 1: A full-thickness disc of skin (2 cm diameter) was removed from each inner calf of a human volunteer. Each wound was allocated an identical treatment device, one active and the other placebo. The identity of the device was revealed only when the wounds had completely healed. The devices were worn for 16 h a day until that time. Biopsies of both wounds were performed nine months after healing. The tissue was sectioned and stained with either Haematoxylyin + Eosin or Van Gieson. The sections were examined by a histopathologist who was not aware which wound had been actively treated.

Experiment 2: In this double-blind experiment, a series of twenty (3 mm diameter) full-thickness wounds were made on the upper aspect of the thighs of a human volunteer. Ten wounds received placebo treatment, the other ten received active treatment. The pulsed RF devices were similar to the lower power devices used in the rat tensile strength experiment and were worn continuously. Biopsies of the wounds were performed during the initial period of healing, at 1, 2, 3, 5, 7, and 14 days. The results shown below are a summary of all of time groups.

Device specification
Power source 3.5 V battery
Carrier frequency 44 MHz
Pulse width 100 µs
Pulse repetition frequency 1 kHz

Results
Experiment 1:

The placebo side was characterized by a thin epidermal layer (see Fig. 1, side B) and showed other features of normal secondary wound healing:

(i) Basal epidermal layer pleomorphism.
(ii) Lack of pallisading.
(iii) Endarteritis.

The placebo-treated wound took 54 days to heal. In contrast, the actively treated wound showed an almost normal depth of epidermal layer (see Fig. 1, side A) and other advantageous features not usually associated with secondary wound healing:
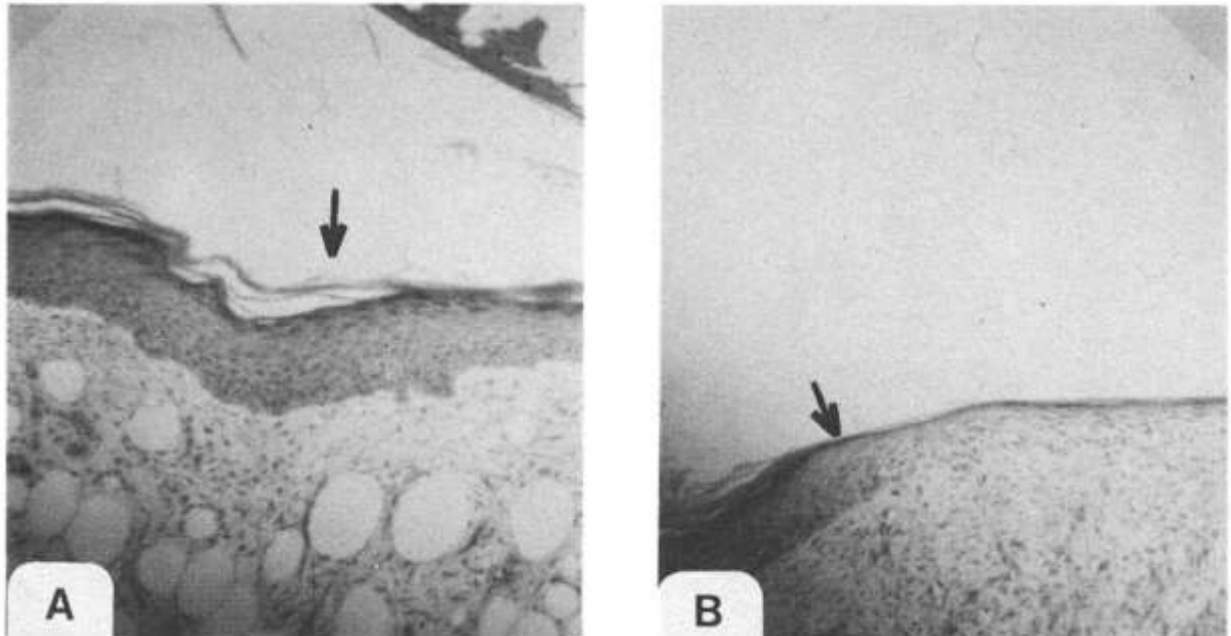
Fig. 1. Epidermal layer of repaired human punch skin wound. (A) Actively treated wound; (B) placebo-treated wound. (Arrows indicate the wound edges.)

(i) No pleomorphin.
(ii) Basal cell pallisading.
(iii) No endarteritis, but developed endothelium.
The actively treated wound took 39 days to heal.

Experiment 2:
As with the first experiment the placebo-treated wounds showed the typical features of secondary wound healing:
(i) Thin epidermia.
(ii) Basal-layer pleomorphism.
The actively treated wounds showed evidence of:
(i) Earlier epidermal budding.
(ii) Earlier migration into the wound.
(iii) Earlier appearance of rete ridges.
(iv) Almost normal depth of final epidermis.

Conclusions
Treatment of skin wounds with pulsed radio-frequency energy influenced the processes of acute secondary wound healing. The rate of healing was accelerated and the histological appearance of the actively treated wounds showed that the healed epidermis was more like normal skin than the scar tissue typical of secondary wound healing.

MENINGOMYELOCELE STUDY

Introduction

A meningomyelocele is a hernial protrusion of the meninges and spinal cord roots through a bony defect in the vertebral column. Some infants are born with this condition, requiring surgical closure of the defect within the first few days of life. One of the complications of the procedure is dehiscence of the wound (due to the tension of the skin across the operative site). The meninges may become exposed, thus providing a route for infection which may lead to ascending meningitis. This can end in mortality. The purpose of this study was to determine the effects of pulsed RF energy on the integrity of surgical closure of this defect. If treatment with pulsed RF fields leads to a reduction in oedema then tissue tension would be lower and there would be a reduced likelihood of the wounds breaking down.

Method

A prospective study was started in 1974. It ran for seven years and involved 90 patients. The surgical procedure was performed by the same surgeons throughout the duration of the study. This study was not double-blind, a retrospective study of the previous 470 cases performed in the unit confirmed a wound breakdown rate of 7%. The pulsed RF devices were placed over the wound dressings post-operatively and treatment lasted for 16 h a day until four weeks after surgery. Written assessments of all the wounds were completed daily and photographic confirmation of the post-operative course of some wounds was collected by ward staff. Neurological status was assessed by physiotherapists before and after surgery and at regular intervals thereafter.

Device Specifications

Specifications for the device used in this study are not available.

Results

In the first 90 patients entered into the study, the incidence of wound breakdown was significantly reduced from 7% to 0% ($X 2 = 6.67$, $p = 0.01$).

Conclusions

Wound breakdown following meningomyelocele closure with its attendant risk of sending meningitis was eliminated. There were no obvious alterations in surgical technique or in post-operative care that might have accounted for the reduction in wound breakdown. These results suggest a considerable benefit to be derived from treatment with pulsed RF energy and clearly warrant further investigations under double-blind conditions.

BLEPHAROPLASTY STUDY

Introduction

The surgical procedure of blepharoplasty may be performed under general or local anesthesia and involves removal of excess skin and fat from the upper and/or lower eyelids. The low tension in the skin of the peri-orbital region means that post-operative oedema and bruising are inevitable. It is an ideal clinical model for double-blind evaluation of pulsed RF treatment because it provides asymptomatic patients who each undergo a bilateral procedure performed by a single surgeon; the patient acts as his or her own control.

A double-blind pilot study has been reported previously [35]. In the pilot study no attempt was made to obtain any numerical estimates of oedema and bruising on which to perform statistical analysis. The purpose of the present study was to replicate the clinical effect observed in the pilot study and to quantify that effect using a larger sample of patients.

Method

The subjects of this clinical study were the patients of a plastic surgeon (Mr . F.V. Nicolle) practicing in London, England. All patients attending for bilateral blepharoplasty who gave their informed consent to participation were entered into the study; there were no specific exclusion criteria. Patients receiving surgery to the upper lids and/or the lower lids were included.

Patients were randomly assigned a pair of special lens less spectacles to provide treatment to the lids of one eye but not the other. Active and placebo antennae were fitted into the light weight spectacle frames and electrical components were housed in one leg of the frames. The placebo antenna was electrically shielded to prevent re-radiation from the active antenna which emitted pulsed RF energy of the following specifications:

Nominal power output 73 µW
Carrier frequency 26 MHz
Pulse width 73 µs
Pulse repetition frequency 900 Hz

Patients therefore acted as their own control and they were not aware which eye received treatment. Treatment commenced immediately following surgery and the patients were instructed to wear the spectacles for 16 h per day for the following three days. Apart from this no modifications were made to the normal post-operative care of the patients. Patients were asked to keep a log, on a small card provided, of the hours for which they wore the spectacles. At each post-operative visit, that is at one day (a few cases only) and at three, four of five days after surgery, the nurse took a clinical photograph which was developed into a color slide. The clinical logistics of the study precluded the taking of absolutely standard photographs. Therefore, in order to be able to make a correction to the measurements for the absolute size of each photograph, it was decided to place a centimeter scale reference sticker on the forehead of each patient prior to the clinical photograph being taken . Unfortunately this decision was not taken until after the first twelve patients had been entered into the study.

Measurements

The slides were used to obtain measurements of bruising and the amount each eye was open and they were also clinically assessed by a panel of three judges (one surgeon, one nurse and one lay person).

The bruising beneath each eye was recorded by projecting the slide onto a piece of acetate film and then drawing a planimetric trace of the bruised regions below the median palpebral tissue on each side. Only the areas of clearly defined red or purple bruising were included, not the rather diffuse areas of yellow. A System III Image Analysis Machine (AMS Limited) was then used to measure the area (in square centimeters) of the planimetric trace beneath each eye.

The slides were then projected onto a white piece of paper on which two thin black "+" signs had been drawn. The height of the palpebral fissure of each eye (at the point of bisection of the pupil) and the size of the centimeter scale reference sticker (when present) were marked off on the "+" signs with a thin pencil. The paper was then laid flat to enable the amount each eye was

open and the length of the scale reference sticker to be measured with a ruler. To obtain ratings of the extent of oedema, bruising and scleral hemorrhage, the three assessors examined the projected slides and recorded a rating of each clinical sign on a specially prepared form . The eyes were rated on the following scale for each sign:

2R The patient's RIGHT eye shows *significantly less* than the _ _ _ _ patient's LEFT eye.
1R The patient's RIGHT eye shows less _ _ _ _ _ _ _ _ _ _ _ _ _ _ than the patient's LEFT eye but this is of *little clinical significance* .
0 There is no discernable difference between the patient's LEFT and RIGHT eyes with respect to _ _ _ _ _ _ _ _ _ _ _ _
2L The patient's LEFT eye shows *significantly less* _ _ _ _ _ _ _ _ _ _ _ than the patient's RIGHT eye.
1L The patient's LEFT eye shows less _ _ _ _ _ _ _ _ _ _ _ _ _ _ _than the patient's RIGHT eye but this is of *little clinical significance*.
All of the Day 3 (4 or 5) photographs were assessed before any of the Day 1 photographs and the three assessors were blind as to the side of treatment of each patient.

Analyses

Bruising and eye-opening data were analyzed using related samples t tests and contingency tables were drawn up of the clinical assessment data and submitted to X^2 tests of association.

Patients who failed to return the log of the times the spectacles had been worn or who wore the spectacles for fewer than 8 h per day for at least two days were excluded from the analysis.

Because not all of the pictures were taken with the patients wearing a scale reference sticker it was not possible to provide a correction factor to the measurement data in every case. Two analyses were therefore performed. To include all patients, the data was transformed to the percentage of total bruising or eye opening
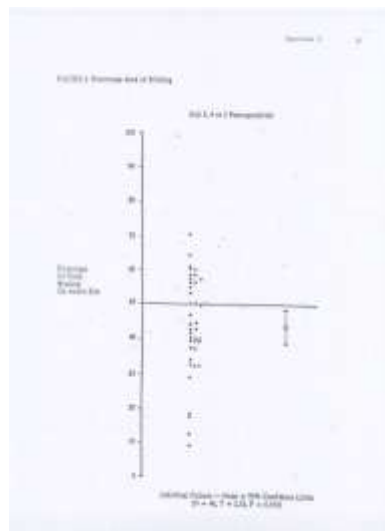
Fig. 2 . Percentage of total bruising which was on the active side (Day 3, 4 or 5 post-operatively). Graph shows individual score for each patient and the group mean (± 95% confidence intervals).

which was on the active side. The second analysis, which used the measured size of the scale reference sticker to convert the bruising data to actual areas, is considered to give a more meaningful picture even though it included fewer patients.

Results

There were a total of sixty patients available for analysis in the present study. Two of these patients failed to return the log of the times when the spectacles were worn, two had worn the spectacles for fewer than the required 2 days and fourteen had worn the spectacles for fewer than the required 8 h per day . There were thus forty-two patients entered into the analyses, of whom nine patients had slides from Day 1 Post-operation and of these two had slides from Day 1 only.

Figure 2 shows the area of bruising on the actively treated side as a percentage of the total bruising of both sides . It can be seen that for the patients as a whole the percentage of the total bruising which was on the active side was significantly less
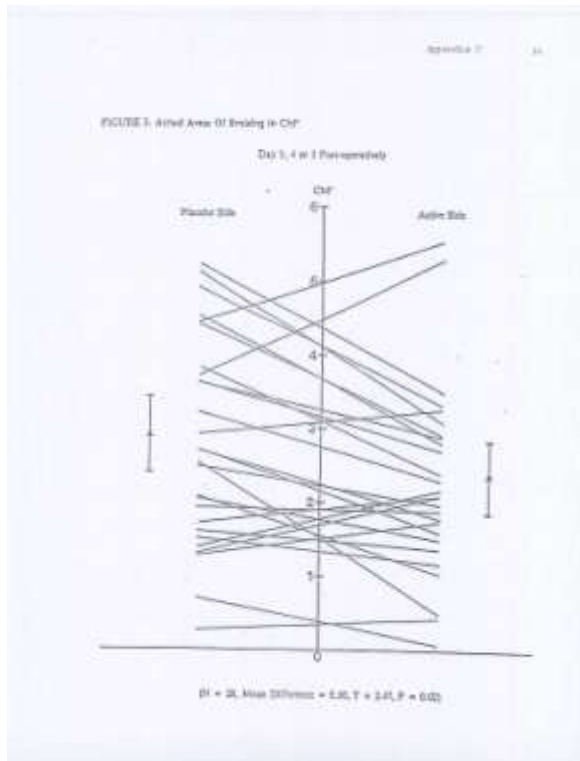
Fig. 3. Actual areas of bruising on the actively treated side and the placebo side (Day 3, 4 or 5 post-operatively). Graph shows the scores for each patient and the group means (±95% confidence intervals).

than 50%, which is the outcome which would be expected to occur by chance (I = 2.56, p = 0.015). This is equivalent to a mean reduction in bruising on the active side of 20 .7% (95% confidence interval, 5.2% to 33.8%).

For the 28 patients who had worn the scale reference sticker it was possible to convert the bruised area measurements to actual areas. Figure 3 shows these results. It can be seen that

the mean area of bruising on the placebo side was 2 .88 cm2 and for the active side it was 2.38 cm2. This difference was again statistically significant (t = 2 .47, p = 0.02) and indicates that there was 17.4% less bruising on the actively treated side (95% confidence interval, 3 .7% to 31%).

Figures 4 and 5 show, for the Day 1 and Day 3, 4 or 5 photographs respectively, the height of the palpebral fissure of the actively treated side as a percentage of the combined heights of the palpebral fissures of both sides. In neither case is this value significantly different from 50% (Day 1 : t = 0 .52, NS; Day 3, 4 or5 : t = 0.62, NS).

Although the clinical sign of oedema is more striking on the first day following surgery, too few patients with Day 1 photographs were available to permit a meaningful analysis of the clinical assessments of them. Even for the Day 3, 4 or 5 photographs there were not sufficient patients to perform a reliable analysis of the full five assessment levels. However, by combining the two levels of assessment on each side (2R and 1R, and 2L and 1L) and excluding the small number of cases assessed as showing no difference, the cell entries are large enough to permit meaningful conclusions (see Table 2). It can be seen that there is a strong

TABLE 2. Clinical Assessment of Oedema by Surgeon Assessor (Table combining assessment levels).

	Less Oedema on Left	Less Oedema on Right	Total
LEFT SIDE ACTIVE	12	5	17
RIGHT SIDE ACTIVE	5	13	18
TOTAL	17	18	35

association between the clinical assessments made and the side of activity of the spectacles that the patient was wearing (Pearson $X 2$ = 6.4, p = 0 .01). Table 3 similarly shows the same surgeon's assessments of the patients' bruising. Again the association between assessments made and side of activity of the spectacles worn is statistically significant (Pearson $X 2$ = 5.9, p = 0.015). Only six patients show any scleral hemorrhage and there is no evidence of its presence being associated with the side of activity of the spectacles being worn (Pearson $X2$= 1 .3, NS).

The results of the other two assessors were in broad agreement with the findings of the surgeon, though, with more assessments being recorded as no discernable difference, the same levels of significance were not attained.

Discussion

The results of the present study provide objective evidence for and statistical underpinning of the clinical impressions reported in the pilot study. After approximately three days of post-operative treatment with low levels of pulsed RF energy there is a clear reduction in the area of

bruising and in the observable signs of oedema around the treated eye in comparison with the untreated eye.

TABLE 3. Clinical Assessment of Bruising by Surgeon Assessor (Table combining assessment levels).

	Less Bruising on Left	Less Bruising on Right	Total
LEFT SIDE ACTIVE	12	4	16
RIGHT SIDE ACTIVE	6	12	18
TOTAL	18	16	34

GENERAL DISCUSSION

Four studies have been described which provide support, from both laboratory and clinical research environments, for the contention that pulsed RF fields may be of value in the treatment of soft tissue-injuries. Furthermore, the hypothesis that such effects may be mediated through a reduction in oedema has been upheld. As argued in the introduction, the influence of oedema, which occurs during the inflammatory reaction phase of wound healing, may extend beyond this phase and result in lower wound tensile strength and delay the onset of collagen synthesis [34]. The laboratory study of rat abdominal wound repair has indeed demonstrated that tensile strength is more developed in the groups treated with pulsed RF energy. Further evidence that the physiological events of the reparative phase of wound healing occur earlier following treatment with pulsed RF fields was found in the human skin wound experiments; the first experiment showed an improved end result and in the second experiment histological evidence of repair appeared earlier in the treated wounds. That these effects were not confined to the laboratory setting was demonstrated in the meningomyelocele study in which wound breakdown following surgery was eliminated. This might have been due to improved tensile strength of the wound or to a reduction in oedema creating a lower bursting pressure (or both), although it must be stressed that this was not a randomized control trial. Finally, in the blepharoplasty study direct evidence has been obtained that pulsed RF treatment reduces both bruising and oedema. Oedema is produced by changes in micro vascular permeability, by the breakdown of extravagated proteins (which increases tissue osmotic pressure), by increased capillary blood pressure and by increased fluidity of the tissue ground substance (preventing the rise in tissue tension which opposes further release of exudate) [25]. One possible mechanism of action of the pulsed RF fields might be to prevent the disaggregation of the mucopolysaccharides of ground substance which causes its increased fluidity and is one of the earliest features of the inflammatory response. In this way the fluid exudate and free red blood cells from the damaged capillaries would be less able to spread from the initial site of injury. It is interesting in this context to note that attempts to model the effects of electric fields on connective tissue [36] have concentrated on the polysaccharides (GAGs) which are the main charge-bearing constituents.

CONCLUSIONS

The body of research into the effects of treatment of wounds with pulsed RF fields has demonstrated:

(i) Earlier appearance of tensile strength.

(ii) Evidence of earlier onset of reparative processes in secondary wound healing.

(iii) Reduced bruising and oedema is primary wound healing.

It may therefore be concluded that treatment with pulsed RF or similarly configured devices can accelerate some processes of primary and secondary wound healing. It is not proven that these effects are mediated through a reduction of interstitial oedema; there may be a number of separate mechanisms involved.

REFERENCES

1 E. Fukada and I. Yasuda, 1. Phys. Soc. Jpn., 12 (1957) 1158.

2 R.O . Becker, Science, 134 (1961) 101.

3 C.A.L. Bassett and R.O. Becker, Science, 137 (1962) 1063.

4 R.H.C . Bentall, Br. J. Cancer, 45 (1982) Suppl. V, 82.

5   R.H.C . Bentall in Charge and Field Effects in Biosystems, M .J. Allen and P .N .R. Usherwood (Editors),   Abacus Press, Kent, 1984, pp . 331-351.

6 M. Nadashi, Am. J. Orthop., 2 (1960) 105.

7 B .M. Cameron, Am. J. Orthop., 3 (1961) 336 .

8 B .M. Cameron, Am. J. Orthop., 6 (1964) 72.

9 J.E. Fenn, Can. Med. Assoc. J., 100 (1969) 251 .

10   J.H. Goldin, N .R .G. Broadbent, J.D. Nancarrow and T. Marshall, Br. J. Plast, Surg., 34 (1981) 267.

11 C.A.L . Bassett, R.J. Pawluk and A.A. Pilla, Science, 184 (1974) 575.

12 J. Watson and E.M. Downes, Med. Biol . Eng. Comput ., 17 (1979) 161 .

13 C .A .L. Bassett, S.N. Mitchell and S .R. Gaston, J. Bone Jt . Surg., 63A (1981) 511.

14 J. Watson, Proc. IFFF, 67 (1979) 1339.

15 C .B . Frank and A.Y.J . Szeto, IEEE Eng. Med. Biol ., 12 (1983) 27 .

16   A.J.H. Rains and H .D. Ritchie in Bailey and Love's Short Practice of Surgery, H.K. Lewis, London, 1977.

17   R. Marks in Tissue Repair and Regeneration, L .E. Glynn (editor), Elsevier/North Holland Biomedical Press, Amsterdam, 1981, pp. 309-342 .

18 J.F. Newcombe in Scientific Basis of Surgery, W .T. Irvine (Editor), Churchill Livingstone, London,
        1972, pp. 433-456.

19   P . Pullar in Modem Trends in Forensic Medicine, K.A . Mant (Editor), Butterworths, London, 1973, Vol . 3, pp . 64-92 .

20 G.B . Ryan and G. Majno, Am. J. Pathol., 86 (1977)'185 .

21 J.E . Dunphy and K.N. Udupa, N . Engl. J. Med ., 253 (1955) 847.

22 T.K . Hunt, World, J. Surg., 4 (1980) 271.

23 L.E. King, J. Invest. Dermatol., 84 (1985) 165 .

24 D. Montandon, G . D'Andrian and G. Gabbiani, Clin . Plast. Surg., 4 (1977) 325.

25   J.B. Walter and M.S . Israel in General Pathology, 3rd ed., Churchill Livingstone, London, 1972, pp. 167-189.

26 C .A. Keele and E. Neil, Samson Wright's Applied Physiology, Oxford University Press, London,
        1971.

27 A. Leaf, Circulation, 48 (1973) 455.

28 M.A. Shields and H.A.F. Dudley, Br. J. Surg., 158 (1971) 598.

29 E.M. Landis, Ann. N. Y. Acad. Sci., 46 (1946) 713.

30 S . Sevitt, J. Pathol. Bacteriol., 75 (1958) 27.
31 S. Sevitt, J. Pathol. Bacteriol., 61 (1949) 427.
32 J .P. Remensnyder, Arch. Surg., 105 (1972) 477.
33 D.P. Speer, J. Surg. Res., 27 (1979) 385.
34   E.E. Peacock and W. Van Winkle, Wound Repair, Saunders. Philadelphia, 1976, pp . 1- 21, 145-02, 215-231.
35 F .V. Nicole and R.H.C . Bentall, Aesthet. Plast. Surg., 6 (1982) 169.
36 A.J . Grodzinsky, CRC Crit. Rev. Biomed. Eng., 9 (1983) 133.

Confirming Animal Studies

In 2011 a significant study* on the healing of wounds in diabetic mice confirmed the initial finding of Dr. Bentall on experimental wounds in humans and rats. In this recent study full-thickness cutaneous wounds were made in db/db mice (diabetic mouse model), with one group treated with PRFE and a sham treated control group. The PRFE treatment was delivered by a higher power device twice daily for 30 min. However, detailed analysis of the wounds showed the treated group had accelerated wound healing through wound contraction via stimulating cell proliferation, granulation tissue formation and collagen deposition. These studies confirm the findings outlined by Dr. Bentall on wound healing and show that PRFE promotes wound healing, but that extended time PRFE treatments and higher power short time PRFE treatments, have the same impact on healing of full thickness cutaneous wounds.

* Qin Li, , Huangkai Kao, Evan Matros, , Cheng Peng, George F.
Murphy, Lifei Guo. Pulsed Radio Frequency Energy (PRFE) Accelerates Wound Healing In Diabetic Mice Plast Reconstr Surg. 2011 Jun;127(6):2255-62.

Extended time low power clinical studies

The studies by Dr. Bentall laid the ground work for further development of PRFE device that are small portable and offer a significant therapeutic benefit. The studies below were carried by a variety of extended use PRFE devices. Titles and abstracts are shown:

Frederick V. Nicolle, M. Chir. and Richard M. Bentall Use of Radio-Frequency Pulsed Energy in the Control of Postoperative Reaction in Blepharoplasty Aesth. Plast. Surg. 6:169-171, 1982

This is a preliminary report of the use of a device to apply small pulses of radio-frequency energy to surgical wounds in order to improve wound healing. The device was applied to one eye in 21 patients who underwent bilateral blepharoplasty. There were no device related complications. In l l patients, edema and ecchymosis were noticeably less on the treated side within 24 hours of surgery. In 6 patients, ecchymosis and swelling were so slight that no difference between treated and untreated sides was visible. Two patients were noticeably worse on the treated side. Further studies will be conducted.

Foley-Nolan D, Moore K, Codd M, Barry C, O'Connor P, Coughlan RJ. Low energy high frequency pulsed electromagnetic therapy for acute whiplash injuries. A double blind randomized controlled study. Scand J Rehabil Med. 1992;24(1):51-9.

The standard treatment of acute whiplash injuries (soft collar and analgesia) is frequently unsuccessful. Pulsed electromagnetic therapy PEMT (as pulsed 27 MHz) has been shown to have pro-healing and anti-inflammatory effects. This study examines the effect of PEMT on the acute whiplash syndrome. One half of the 40 patients entering the study received active PEMT collars: the other half facsimile (placebo). All patients were given instructions to wear the collar for eight hours a day at home and advised to mobilise their necks. At 2 and 4 weeks the actively treated group had significantly improved (p less than 0.05) in terms of pain (visual analogue scale). By chance movement scores for the PEMT group were significantly worse at entry to the study than the control group (p less than 0.05). At 12 weeks they had become significantly better (p less than 0.05). PEMT as described is safe for domiciliary use and this study suggests that PEMT has a beneficial effect in the management of the acute whiplash injury.

Foley-Nolan D, Barry C, Coughlan RJ, O'Connor P, Roden D Pulsed high frequency (27MHz) electromagnetic therapy for persistent neck pain. A double blind, placebo-controlled study of 20 patients. Orthopedics. 1990 Apr;13(4):445-51.

In the majority of patients with neck pain, symptoms will resolve spontaneously or quite quickly in response to therapy. However, some patients' symptoms persist for a long period, irrespective of therapy. In this study, 20 patients with persistent (greater than 8 weeks) neck pain were enrolled in a double blind, placebo-controlled trial of low energy, pulsed electromagnetic therapy (PEMT)--a treatment previously shown to be effective in soft tissue injuries. For the first 3-week period, group A (10 patients) received active PEMT units while group B (10 patients) received facsimile placebo units. After 3 weeks, both pain (visual analogue scale (P less than .023) and range of movement (P less than .002) had improved in the group on active treatment compared to the controls. After the second 3 weeks, during which both groups used active units, there were significant improvements in observed scores for pain and range of movement in both groups. PEMT, in the form described, can be used at home easily in the treatment of patients with neck pain. It is frequently successful and without side effects.

Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol. 1992 Aug;127(2):147-54.

A prospective, randomized, double-blind, placebo-controlled multicenter study assessed the clinical efficacy and safety of pulsed electromagnetic limb ulcer therapy (PELUT) in the healing of recalcitrant, predominantly venous leg ulcers. The portable device was used at home for 3 h daily during this 8-week clinical trial as an adjunct to a wound dressing. Wound surface area,

ulcer depth and pain intensity were assessed at weeks 0, 4 and 8. At week 8 the active group had a 47.7% decrease in wound surface area vs. a 42.3% increase for placebo (P < 0.0002). Investigators' global evaluations indicated that 50% of the ulcers in the active group healed or markedly improved vs. 0% in the placebo group, and 0% of the active group worsened vs. 54% of the placebo group (P < 0.001). Significant decreases in wound depth (P < 0.04) and pain intensity (P < 0.04) favoring the active group were seen. Patients whose ulcers improved significantly after 8 weeks were permitted to continue double-blind therapy for an additional 4 weeks. Eleven active and one placebo patient continued therapy until week 12, with the active treatment group continuing to show improvement. There were no reports of adverse events attributable to this device. We conclude that the PELUT device is a safe and effective adjunct to non-surgical therapy for recalcitrant venous leg ulcers.

Hedén P, Pilla AA. Effects of pulsed electromagnetic fields on postoperative pain: a double-blind randomized pilot study in breast augmentation patients. Aesthetic Plast Surg. 2008 Jul;32(4):660-6.

Postoperative pain may be experienced after breast augmentation surgery despite advances in surgical techniques which minimize trauma. The use of pharmacologic analgesics and narcotics may have undesirable side effects that can add to patient morbidity. This study reports the use of a portable and disposable noninvasive pulsed electromagnetic field (PEMF) device in a double-blind, randomized, placebo-controlled pilot study. This study was undertaken to determine if PEMF could provide pain control after breast augmentation. Forty-two healthy females undergoing breast augmentation for aesthetic reasons entered the study. They were separated into three cohorts, one group (n = 14) received bilateral PEMF treatment, the second group (n = 14) received bilateral sham devices, and in the third group (n = 14) one of the breasts had an active device and the other a sham device. A total of 80 breasts were available for final analysis. Postoperative pain data were obtained using a visual analog scale (VAS) and pain recordings were obtained twice daily through postoperative day (POD) 7. Postoperative analgesic medication use was also followed. VAS data showed that pain had decreased in the active cohort by nearly a factor of three times that for the sham cohort by POD 3 (p < 0.001), and persisted at this level to POD 7. Patient use of postoperative pain medication correspondingly also decreased nearly three times faster in the active versus the sham cohorts by POD 3 (p < 0.001).Pulsed electromagnetic field therapy, adjunctive to standard of care, can provide pain control with a noninvasive modality and reduce morbidity due to pain medication after breast augmentation surgery.

Rohde C, Chiang A, Adipoju O, Casper D, Pilla AA. Effects of pulsed electromagnetic fields on interleukin-1 beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients. Plast Reconstr Surg. 2010 Jun;125(6):1620-9.

Surgeons seek new methods of pain control to reduce side effects and speed postoperative recovery. Pulsed electromagnetic fields are effective for bone and wound repair and pain and edema reduction. This study examined whether the effect of pulsed electromagnetic fields on

postoperative pain was associated with differences in levels of cytokines and angiogenic factors in the wound bed. In this double-blind, placebo-controlled, randomized study, 24 patients, undergoing breast reduction for symptomatic macromastia received pulsed electromagnetic field therapy configured to modulate the calmodulin-dependent nitric oxide signaling pathway. Pain levels were measured by a visual analogue scale, and narcotic use was recorded. Wound exudates were analyzed for interleukin (IL)-1 beta, tumor necrosis factor-alpha, vascular endothelial growth factor, and fibroblast growth factor-2. Pulsed electromagnetic fields produced a 57 percent decrease in mean pain scores at 1 hour ($p < 0.01$) and a 300 percent decrease at 5 hours ($p < 0.001$), persisting to 48 hours postoperatively in the active versus the control group, along with a concomitant 2.2-fold reduction in narcotic use in active patients ($p = 0.002$). Mean IL-1 beta concentration in the wound exudates of treated patients was 275 percent lower ($p < 0.001$). There were no significant differences found for tumor necrosis factor-alpha, vascular endothelial growth factor, or fibroblast growth factor-2 concentrations. Pulsed electromagnetic field therapy significantly reduced postoperative pain and narcotic use in the immediate postoperative period. The reduction of IL-1 beta in the wound exudate supports a mechanism that may involve manipulation of the dynamics of endogenous IL-1 beta in the wound bed by means of a pulsed electromagnetic field effect on nitric oxide signaling, which could impact the speed and quality of wound repair.

Ian M Rawe, Tracey C Vlahovic. The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: a case report. Int Wound J 2011. In press

Pulsed radio frequency energy (PRFE) has successfully been used to treat diabetic and venous stasis ulcers. In this case report, a lightweight wearable form of a PFRE device was evaluated and used to treat three diabetic foot ulcers and one venous stasis ulcer. The ulcers were present on the four patients for more than 3 months and had failed to heal after conventional treatment. A lightweight battery-powered, wearable form of PRFE device was introduced as a treatment and used 6–8 hours per day for a period of 6 weeks. All patients after 1 week of therapy showed improvement and wound size was seen to decrease. Patient 1 had a venous stasis ulcer, and reported significant pain relief after 2 weeks treatment. Patients 2 and 3 achieved complete healing after 3 weeks treatment, and patients 1 and 4 had a 95% and 88% reduction in wound size, respectively, after the 6-week study period. Both these patients continued to complete healing using the PRFE device after the 6-week study period. PRFE treatment delivered in the form of a wearable lightweight patch appears to offer promise in the treatment of recalcitrant chronic wounds.

I. M. Rawe, , A.Lowenstein,. C. Raul Barcelo, D. G Genecov. Control of postoperative pain with a wearable continuously operating pulsed radio frequency energy device – a preliminary study. Aesthetic Plast Surg (under review)

Pulsed radio frequency energy (PRFE) has long been reported to have a therapeutic effect on postoperative pain. In this study, a portable, wearable, low energy emitting form of PRFE

therapy device was used to determine the control of postoperative pain following breast augmentation surgery. Eighteen healthy women who underwent breast augmentation entered the study, the procedure performed purely for aesthetic considerations. Postoperative pain following surgery was assessed with a 0-10pt visual analogue scale (VAS). Baseline pain scores were taken on completion of the operation and patients were randomly assigned coded PRFE devices, which were either Active devices or Placebo devices. VAS scores were recorded twice daily for seven days (am and pm). Medication use was also logged for 7 days. The PRFE devices were left in place and in continual operation for the 7 days of the study. All patients tolerated the PRFE therapy well and there were no reported side-effects. VAS scores for the Active group were significantly lower on postoperative day 1. By day 7 the percent of the baseline VAS remaining in the Active group was 7.9%, compared to the Placebo group of 38%. Along with lower VAS scores, narcotic pain medication use was lower in the patient group who received PRFE therapy. Postoperative pain is significantly lower with PRFE therapy. PRFE therapy in this form is an excellent, drug free and safe method of postoperative pain control.

The Future

These studies have demonstrated that extended wear PRFE have therapeutic benefit that is equivalent to the larger power, short treatment time devices. With continued innovation the concept of extended use wearable PRFE devices can now be fully realized. Overcoming many obstacles Bioelectronics Corporation now offers very small PRFE devices that can be worn comfortably for extended periods. They are used for musculoskeletal pain, postoperative pain, and menstrual pain and promote healing of chronic wounds. A series of clinical studies have been carried out demonstrating both safety and efficacy and these studies are present in the following section.

BioElectronics Clinical Studies

The following clinical studies support our claims for the control of pain, inflammation and edema.

The study presented below has been submitted to the Aesthetics of Plastic surgery and is under peer review. The study shows the control of postoperative pain following surgery. This study is very similar to and almost replicates a previously published study using an IVIVI technologies PRFE device, which has similar characteristics to the BioElectronics PRFE device. (Heden et al. 2008)

CONTROL OF POST-OPERATIVE PAIN WITH A WEARABLE CONTINUOUSLY OPERATING PULSED RADIO FREQUENCY ENERGY DEVICE

Aesth Plast Surg.in press

Ian M. Rawe, Ph.D[1], Adam Lowenstein, [3]

C. Raul Barcelo, MD[2], David G Genecov MD[2]

1. Consultant, BioElectronics Corporation,

2. Private Practice in Dallas, Texas

3. Private Practice in Santa Barbara, California

Short title: pulsed radio frequency: postoperative control of pain

Introduction

Pulsed radio frequency energy (PRFE) has long been reported to have a therapeutic effect on postoperative pain. In this study, a portable, wearable, low energy emitting form of PRFE therapy device was used to determine the control of postoperative pain following breast augmentation surgery.

Methods

Eighteen healthy women who underwent breast augmentation entered the study, the procedure performed purely for aesthetic considerations. Postoperative pain following surgery was assessed with a 0-10pt visual analogue scale (VAS). Baseline pain scores were taken on completion of the operation and patients were randomly assigned coded PRFE devices, which were either Active devices or Placebo devices. VAS scores were recorded twice daily for seven days (am and pm). Medication use was also logged for 7 days. The PRFE devices were left in place and in continual operation for the 7 days of the study.

Results

All patients tolerated the PRFE therapy well and there were no reported side-effects. VAS scores for the Active group were significantly lower on postoperative day 1. By day 7 the percent of the baseline VAS remaining in the Active group was 7.9%, compared to the Placebo group of 38%. Along with lower VAS scores, narcotic pain medication use was lower in the patient group who received PRFE therapy.

Conclusion

Postoperative pain is significantly lower with PRFE therapy. PRFE therapy in this form is an excellent, drug free and safe method of postoperative pain control.

Key Words: Pulsed radio frequency, postoperative, pain

Introduction

Postoperative pain following is surgery is a major priority for both patients and doctors. Pain affects blood pressure, heart rate, appetite, and general mood. Despite advances in our understanding of the neurobiology of nociception, development of new analgesics, and refining minimally invasive surgical techniques, postoperative pain continues to be under-treated[1]. A 2003 survey of pain management in the USA shows that there is still a need to enhance postoperative pain management[2]. The improvement of effective analgesia in the early postoperative period may lead to clinically important benefits regarding long term recovery, including decreasing the incidence of chronic post-surgical pain[3]. Chronic pain, for example, following breast cancer surgical treatment is a major clinical problem, affecting 25 to 60% of patients[4]. An added benefit of improved analgesia is enhanced recovery with shortened hospital stays and convalescence[5, 6].

An underused postoperative pain management modality is pulsed radio frequency energy (PRFE) therapy, also known as pulsed electromagnetic field therapy (PEMF), pulsed short wave therapy (PSWT) and RF non-thermal diathermy. In 1947 the Federal Communications Commission assigned three frequencies at the short end of the RF band for medical use (40.68 MHz, 13.56 MHz and 27.12 MHz)[7]. The frequency of 27.12 MHz is the most widely used in clinical practice. The first PRFE device, the Diapulse was commercially available in the 1950's, and was followed by other commercially available machines. As a treatment for non-healing bone fractures in humans, the use of PEMF is well established[8], and has been in use since the 1970's. Clinical studies have demonstrated its safety and efficacy as a treatment for pain, edema and soft tissue injury. Some of the first studies of postoperative edema and edema caused by soft tissue injury showed promising results[9, 10]. Studies on postoperative pain also showed good results[11-13]. The reduction of capsular contraction in 41 patients after breast augmentation surgery was achieved with PRFE therapy along with massage and closed capsulotomy treatment[14]. Pain and edema has also been treated with PRFE therapy in a number of orthopedic conditions[7, 15-18].

PRFE therapy has also been demonstrated to be effective for chronic wounds, including diabetic and venous stasis ulcers. A number of early studies showed good results[19], with improved healing of pressure ulcers with PRFE treatment[20]. A prospective, randomized, double-blind, placebo-controlled multicenter study assessed the clinical efficacy and safety of pulsed electromagnetic therapy delivered by a portable device. The device was used at home in the healing of recalcitrant, predominantly venous leg ulcers. Significant decreases in wound depth and pain intensity favoring the active group were seen[21]. Important recent studies on the use of PRFE for the treatment of chronic wounds may bring a new focus to its application in this field[22-25], including a retrospective study on the Regenesis Biomedical wound healing registry[24] (Regenesis Biomedical, Scottsdale, AZ).

Two studies on postoperative pain using a wearable form of PRFE from Ivivi Technologies have been reported (SofPulseTM, Ivivi Technologies, Northvale, NJ). A double blind placebo controlled, randomized clinical trial on breast augmentation showed a significant decrease in postoperative pain[26]. A second study using the same form of wearable PRFE

device following breast reduction surgery also showed significant control of postoperative pain[27]. In this study a decrease in interleukin 1-☐ was reported, suggesting a modulation of the wound healing process. A potential mechanism of action PRFE therapy has been put forward and is reviewed by Straub et al. [28]. And recent reports have further contributed to the understanding of the mechanisms of PRFE therapy on wound healing [29, 30].

Figure 1.

The latest version of PRFE device. The therapeutic field lies within the 12cm antenna. The control module containing the battery is small (4.2 cm x 2.0 cm, with a depth of 0.3 cm) and stream lined allowing for comfortable application.
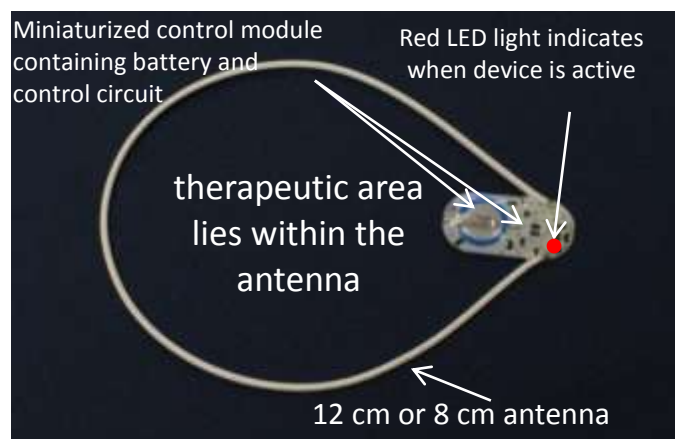
Continued technological advancement has allowed PRFE devices to be produced that are smaller and less obtrusive, as shown in Figure 1 (BioElectronics Corp. Frederick, MD). The small size allows them to be potentially applied to most areas of the body. They are inexpensive to produce and easy for both physician and patient to use.

Materials and Methods

Patients

The ethics review board of North Texas Independent Review Board at Medical City, Dallas, Texas approved this study. All patients enrolled in the study signed a consent form.

PRFE Device

The device used in this study was a pulsed radio frequency energy device (RecoveryRx-BioElectronics Corp) that emits a safe form of non-ionizing electromagnetic radiation. The carrier frequency is 27.12 MHz, the assigned FCC medical frequency, and has a pulse rate of 1000 pulses per second and 100 microsecond burst width. Peak burst output power of the 12 cm antenna is approximately 0.0098 watts covering a surface area of approximate 100 cm^2. The circuitry consists of low voltage (3 V) digital/analog electronics that control all timing functions to produce the therapeutic RF field, where the antenna field is placed directly above the therapeutic site.

Study Design

The study was a double blind, placebo controlled randomized study to determine postoperative pain following breast augmentation. The 18 patients recruited into the study had elected the surgery for purely aesthetic reasons. Silicone breast implants (Allergan, Irvine, CA) were used on all patients and each operation was performed under 1 hr. Breast augmentation was performed in the submuscular fashion via either an infra-mammary or peri-areolar approach. Randomization resulted in 10 patients receiving Active devices on each breast and 8 patients receiving Placebo devices on each breast. There were no patient dropouts. The demographics of each patient group were similar with average age, weight and height being very closely matched, 134.4 lbs v 134.1 lbs and age, 32 v 31.3, as well as patient height 5.61 ft v 5.44 ft. Once the surgery was complete the PRFE devices were activated and secured in place with a surgical bra. Placebo devices were activated in the same way and produced a red indicator light showing activation as did the Active devices. Active devices are not felt by the patient, insuring that the patients were unable to determine the treatment group.

Upon completion of the operation a baseline score was assessed for each patient. Pain scores were assessed using a visual analogue scale (VAS) of 0 – 10 pts, with 0 being no pain, and 10 being extreme pain. Pain scores were logged in the am and pm for the 7 days of the study. The use of VAS scores to document pain is well established[31]. Medication use by each patient was also logged. Medications used by patients were opiate based drugs, oxycodone, hydrocodone and propoxyphene.

Statistical analysis

Means with standard deviation are reported. T-tests and repeated measures analyses of variance were used to determine the differences between Active and Placebo groups. The F-test for the equality of variances was performed. A p-value of 0.05 was considered significant.

Results

The PRFE therapy devices were well tolerated by all the patients and there were no adverse effects noted. Data was obtained from all patients and was available for statistical analysis. The baseline score, obtained upon completion of the operation prior to treatment, between the Active group and Placebo group was not significantly different and, therefore, the baseline VAS score was determined from all patients. VAS scores were collected twice daily (am and pm) and were averaged to a daily mean. The mean daily VAS scores and standard deviation are presented in Table 1.

Table 1.

The mean daily VAS scores and standard deviation for the Active group (A-VAS) and the Placebo group (P-VAS) are shown for the seven days of the study.

DAY	P-VAS	A-VAS
(baseline)	6.46 ±1.98	6.46 ±1.98
1	6.80 ±1.74	4.40 ±2.09
2	5.20 ±2.08	3.85 ±2.36
3	5.40 ±2.21	2.57 ±1.32
4	4.25 ±2.37	2.00 ±1.27
5	3.40 ±1.99	1.55 ±1.23
6	3.80 ±2.01	0.75 ±0.65
7	2.40 ±1.02	0.50 ±0.40

The mean baseline VAS score was 6.46 on the 0-10 scale. As shown in Figure 2, the postoperative day 1 VAS scores for the Active group were 2.06 points lower than the baseline score which was significant ($p = 0.02$). The Placebo group VAS scores was 6.80 points, and was not significantly lower than baseline ($p = 0.65$). Comparing the Active group to the Placebo group the Active group had a 2.40 point lower VAS score which was significant with a p value of 0.017.

Figure 2.

At postoperative day 1 the Active group mean VAS score at 4.40, is significantly lower than the 6.46 mean Baseline (p = 0.02) and the 6.80 Placebo mean VAS scores (p = 0.017).

active v baseline p = 0.02
active v placebo p = 0.017
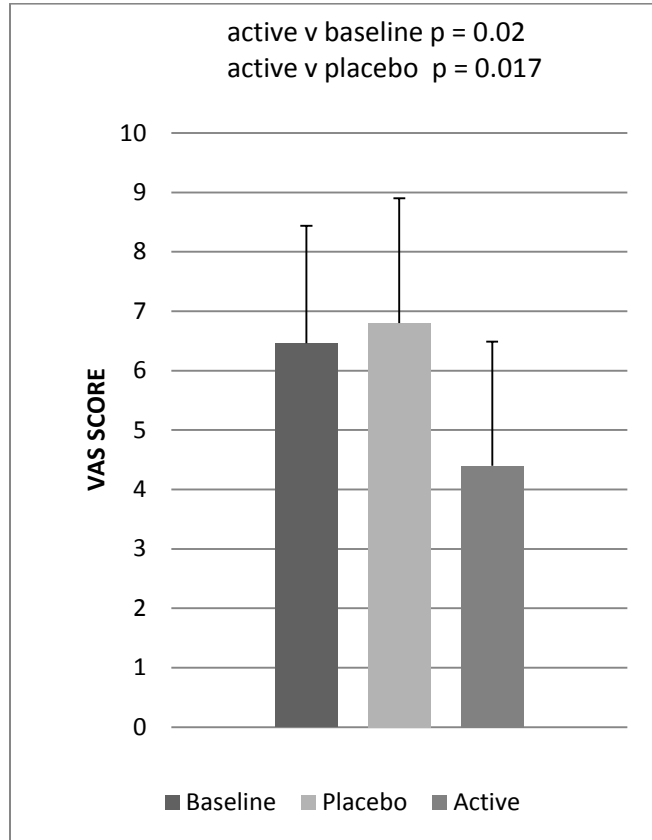
The VAS scores comparing Active to Placebo were significantly different on all days except day 2 (p = 0.23), but was 1.35 VAS points or 35% lower. Figure 3 shows the comparison of the Active and Placebo VAS score to the Baseline at postoperative day 3. At postoperative day 3 the Placebo group VAS is 5.40 points. Comparing Active to Placebo, the Active mean VAS scores is significantly lower than Placebo at day 3 (p = 0.003) with a mean VAS of 2.57 points in the Active group vs 5.40 points in the Placebo group, 2.83 points lower.

Figure 3.

At postoperative day 3 the mean VAS score is 2.83 points lower in the Active group compared to the Placebo group and has recovered 60% from the Baseline score compared to a 17% recovery in the Placebo group (p = 0.003).
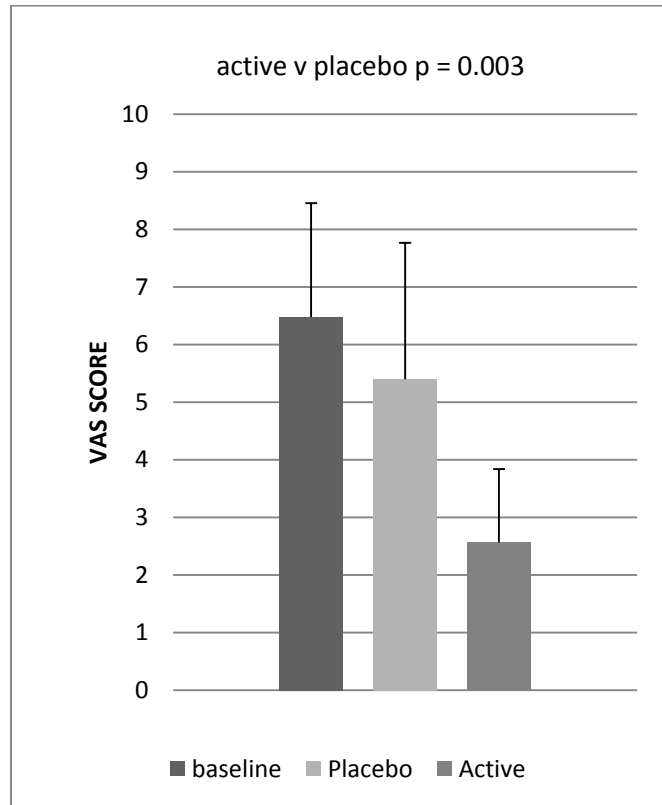
The Active group recovered to 50% of the baseline pain between postoperative days 2 and 3, while the Placebo group recovered to 50% of baseline at postoperative day 6. These results show that the Active group recovers faster than the Placebo group.

Narcotic Pain Medication

The pain medication was logged for by each patient on a daily basis. Patients used both narcotic pain medication consisting of oxycodone 2.5/325 (O),hydrocodone 5/500 (H) , hydrocodone 7.5/500 (H+) and propoxyphene (P).   The total narcotic pain pill use was 145 pills for the Placebo group (H-81, H+9, 0-55) and the Active group 110 narcotic pain pills (H-67, H+-2, O-19.5, P-14.5). The individual patient use of narcotic pain pills in the Active group was as follows: 2.5, 4, 5, 6, 7, 10, 14, 14, 14.5, and 33. In the Placebo group the individual narcotic pill use was 6, 13, 18, 19, 20, 21, 23, and 23. Of the 10 patients in the Active group, 6 patients used 10 or less narcotic pain pills. In the Placebo group, 1 patient used 10 or less. One patient in the Active group used 33 narcotic pain pills (H), this represents 30% of the total of the Active

group narcotic medication use. This is more than twice the level of use than the next highest total (14.5). Statistics for patient use of narcotic medication is shown in Table 2.

Table 2

The total narcotic pills used by patient group, mean, median, standard deviation (SD) and p value, also the total, mean, median, SD and p value with the outlier (italics) removed.

	Total	mean	SD	median	P value	*Total*	*mean*	*SD*	*median*	*P value*
Placebo	145	18.1	5.9	20	-	*145*	*18.1*	*5.9*	*20*	*-*
Active	110	11.0	8.9	8.5	0.07	*77*	*8.5*	*4.6*	*7*	*0.002*

The means were 11.0 pills per patient in the Active group and 18.1 in the Placebo group, representing a 68% increase in narcotic medication use in the Placebo group, though not significant (p = 0.07). However, with the outlier, patient 10 excluded, the mean narcotic pill use becomes 18.1 Placebo and 8.5 in the Active group, showing a significant difference (p = 0.002). The median value, which better controls for any outliers in the data set provides a more representative value for pain pills per patient in the active group. The median for the Active group is 8.5, compared to the median in the Placebo group of 20 prescription pills per patient.

Discussion

Patients who received PRFE therapy experienced significantly less postoperative pain than patients who were assigned the placebo devices. Since VAS scores are a measure of the level of pain, it is interesting to note that by totaling the mean VAS points for each day, results in an accumulated average point total for the Placebo patient group of 31.25 and a total for the Active group of 15.62 VAS points during the 7 day study period. This indicates that the Active group patients experienced, on average, 50% less pain than those who received the Placebo device. This is a considerable decrease in postoperative pain. It must also be considered that the Placebo patients were still experiencing 37% of the baseline VAS score while the active group had 7.7% of the baseline VAS score remaining. Thus the Placebo group would continue to experience significant pain beyond day 7.   This was highlighted by the day 7 Placebo VAS point mean of 2.40 being equivalent to the day 3, 2.57 VAS point mean of the Active group.

The data presented also shows that patients who received PRFE therapy required less narcotic pain medication, which is not surprising, as with lower pain scores less pharmacological pain medication use would be expected. Taken together, decreased postoperative pain and lower narcotic medication use suggests that post-surgical complications would be reduced, and that opiate-related side effects would also be less frequent. These data therefore indicates that the PFRE is an effective and safe method of combating postoperative pain.

Pain medication side effects, opiate-based, acetaminophen and non-steroid anti-inflammatory (NSAID) drugs have been well documented. With opiate drugs these side effects are

postoperative nausea and vomiting, urinary retention, ileus, constipation and sedation. With acetaminophen and NSAID's, side effects, such as hepatic and renal toxicity, coagulation, confusion, sedation and dizziness have been reported. To improve analgesia and combat these side-effects, the concept of multimodal, or balanced analgesia was introduced, with the goal of combining analgesics with additive or synergistic effects[32]. The theory behind this approach is that varying combinations of drugs for managing postoperative pain would improve safety and efficacy due to their different mechanisms of action. There is some indication that this has led to a reduction in opioid-related side effects and improved analgesia [33, 34]. However, patient pain surveys indicate that postoperative pain management is still in need of significant improvement [2, 32]. PRFE energy delivered in this form would add another dimension to the multimodal analgesia approach. However, to be widely used and accepted, the PRFE device needs to be unobtrusive and seamlessly applied to wound dressing and recovery protocols. The RecoveryRx device used in this study is a one-time use disposable device that operates for a minimum of 7 days, requires minimal patient involvement and is very economical to produce. Figure 1 shows the latest version PRFE device, the control module containing the battery measures 4.2 cm x 2.0 cm, with a depth of 0.3 cm. With a 12 cm or 8 cm antenna the device weighs 8 grams and could be simply applied for most surgical recovery protocols without impacting patient comfort while improving outcome. While this study demonstrates the control of postoperative pain, this form of lightweight, wearable PRFE device has also been shown to promote the healing of chronic wounds[25].

The results of the study presented here show control of postoperative pain using a unique, continuously operating low energy PRFE device. The control of postoperative pain is equivalent to the breast augmentation study by Heden et al. with both studies showing significantly lower VAS scores by postoperative day 3 and both studies using portable wearable PRFE devices. However, there are major differences between the two studies. The PRFE device used in the Heden study was the IVIVI Technologies Torino which has a higher peak output at 0.5watts, compared to the RecoveryRX at 9.8 milliwatts. The operation of this IVIVI device follows a protocol of: on initially for 30min every 4 hrs for the first 3 days, then 30 min every 8 hrs for the next 3 days. This contrasts with the continuous operation of the RecoveryRx device used in this study, and shows that continuous low energy application is as effective as shorter treatment time, higher energy devices in controlling postoperative pain. The most significant difference is the physical size of the two PRFE devices used in the studies. The IVIVI Technologies Tourino has a weight of 28 grams, with 15cm or 19cm antenna, and a control module with an approximate size of 6.35 cm by 6.22cm and a depth of 1.68 cm. The weight of the IVIVI device and size of the control module is therefore about 3.5 times greater.

The concept of replacing short high power PRFE energy treatments with extended use low energy treatments was first developed by Dr. Bentall. Dr. Bentall presented data comparing the effects of a 15 Watt PRFE device at 27.12 MHz (Diapulse) to a 2 milliwatt pulsed device at 3 MHz on the tensile strength of rat abdominal wounds[35]. Despite the large difference in the physical size and power output of the two devices, they showed a very similar profile in enhancing the tensile strength of the wounds. The 15 watt Diapulse treatment was given 3 x 20 min per day and the 2 milliwatt treatment was an overnight exposure, control was a 15 Watt light bulb. Applying this concept to postoperative recovery, Nicolle & Bentall demonstrated the

control of edema and bruising during postoperative recovery from blepharoplasty using a low energy, extended use PRFE device.

There is still a need for larger scale clinical trials to further validate this form of postoperative therapy. However, use in a clinical setting of RecoveryRx PRFE therapy has been shown to be as effective as the results presented here. RecoveryRx is estimated to reduce postoperative pain by 60% following caesarean section for example (personal communication Ian Rawe from Charge Nurse, Labor and Delivery Ward).

Given the clear need to improve postoperative analgesia, extended use low energy PRFE devices potentially offer a new dimension to multimodal analgesic techniques. Given that PRFE therapy has a long history of use and that side effects have not been reported. This mode of postoperative analgesia and improved wound healing could be employed in almost all situations, allowing for greater flexibility in the use of pharmacological interventions.

References

1. White, P.F. (2008). Pain management after ambulatory surgery - where is the disconnect? Can J Anaesth *55*, 201-207.
2. Apfelbaum, J.L., Chen, C., Mehta, S.S., and Gan, T.J. (2003). Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg *97*, 534-540, table of contents.
3. Buvanendran, A., Kroin, J.S., Della Valle, C.J., Kari, M., Moric, M., and Tuman, K.J. (2010). Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. Anesth Analg *110*, 199-207.
4. Andersen, K.G., and Kehlet, H. (2011). Persistent Pain After Breast Cancer Treatment: A Critical Review of Risk Factors and Strategies for Prevention. J Pain.
5. White, P.F., and Eng, M. (2007). Fast-track anesthetic techniques for ambulatory surgery. Curr Opin Anaesthesiol *20*, 545-557.
6. White, P.F., Kehlet, H., Neal, J.M., Schricker, T., Carr, D.B., and Carli, F. (2007). The role of the anesthesiologist in fast-track surgery: from multimodal analgesia to perioperative medical care. Anesth Analg *104*, 1380-1396, table of contents.
7. Foley-Nolan, D., Barry, C., Coughlan, R.J., O'Connor, P., and Roden, D. (1990). Pulsed high frequency (27MHz) electromagnetic therapy for persistent neck pain. A double blind, placebo-controlled study of 20 patients. Orthopedics *13*, 445-451.
8. Aaron, R.K., Ciombor, D.M., and Simon, B.J. (2004). Treatment of nonunions with electric and electromagnetic fields. Clin Orthop Relat Res, 21-29.
9. Aronofsky, D.H. (1971). Reduction of dental postsurgical symptoms using nonthermal pulsed high-peak-power electromagnetic energy. Oral Surg Oral Med Oral Pathol *32*, 688-696.
10. Nicolle, F.V., and Bentall, R.M. (1982). Use of radio-frequency pulsed energy in the control of postoperative reaction in blepharoplasty. Aesthetic Plast Surg *6*, 169-171.
11. Benazzo, F., Zanon, G., Pederzini, L., Modonesi, F., Cardile, C., Falez, F., Ciolli, L., La Cava, F., Giannini, S., Buda, R., et al. (2008). Effects of biophysical stimulation in patients undergoing arthroscopic reconstruction of anterior cruciate ligament:

prospective, randomized and double blind study. Knee Surg Sports Traumatol Arthrosc *16*, 595-601.

12.   Till, M., Gubisch, W., Frickert, G., Reichert, H., and Schmidt, K.H. (1993). [Postoperative management with pulsed high frequency electromagnetic energy. A clinical study of 38 patients with rhinoseptoplasty]. Handchir Mikrochir Plast Chir *25*, 26-32.

13.   Frank, R. (1985). Treatment of the perineum by pulsed electro magnetic therapy. Midwives Chron *98*, 297-298.

14.   Silver, H. (1982). Reduction of capsular contracture with two-stage augmentation mammaplasty and pulsed electromagnetic energy (Diapulse therapy). Plastic and reconstructive surgery *69*, 802-808.

15.   Foley-Nolan, D., Moore, K., Codd, M., Barry, C., O'Connor, P., and Coughlan, R.J. (1992). Low energy high frequency pulsed electromagnetic therapy for acute whiplash injuries. A double blind randomized controlled study. Scand J Rehabil Med *24*, 51-59.

16.   Pennington, G.M., Danley, D.L., Sumko, M.H., Bucknell, A., and Nelson, J.H. (1993). Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. Mil Med *158*, 101-104.

17.   Wilson, D.H. (1974). Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. Physiotherapy *60*, 309-310.

18.   Cameron, B.M. (1964). A Three Phase Evaluation of Pulsed, High Frequency, Radio Short Waves (Diapulse): 646 Patients. Am J Orthop *6*, 72-78.

19.   Itoh, M., Montemayor, J.S., Jr., Matsumoto, E., Eason, A., Lee, M.H., and Folk, F.S. (1991). Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus *4*, 24-25, 29-34.

20.   Salzberg, C.A., Cooper-Vastola, S.A., Perez, F., Viehbeck, M.G., and Byrne, D.W. (1995). The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage *41*, 42-44, 46, 48 passim.

21.   Stiller, M.J., Pak, G.H., Shupack, J.L., Thaler, S., Kenny, C., and Jondreau, L. (1992). A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol *127*, 147-154.

22.   Fletcher, S. (2011). Successful treatment of venous stasis ulcers with combination compression therapy and pulsed radio frequency energy in a patient scheduled for amputation. J Wound Ostomy Continence Nurs *38*, 91-94.

23.   Frykberg, R., Martin, E., Tallis, A., and Tierney, E. (2011). A case history of multimodal therapy in healing a complicated diabetic foot wound: negative pressure, dermal replacement and pulsed radio frequency energy therapies. Int Wound J *8*, 132-139.

24.   Frykberg, R.G., Driver, V.R., Lavery, L.A., Armstrong, D.G., and Isenberg, R.A. (2011). The Use of Pulsed Radio Frequency Energy Therapy in Treating Lower Extremity Wounds: Results of a Retrospective Study of a Wound Registry. Ostomy Wound Manage *57*, 22-29.

25.   Rawe, I.M., and Vlahovic, T.C. (2011). The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: A case report. Int Wound J.

26. Heden, P., and Pilla, A.A. (2008). Effects of pulsed electromagnetic fields on postoperative pain: a double-blind randomized pilot study in breast augmentation patients. Aesthetic Plast Surg *32*, 660-666.

27. Rohde, C., Chiang, A., Adipoju, O., Casper, D., and Pilla, A.A. (2009). Effects of Pulsed Electromagnetic Fields on IL-1beta and Post Operative Pain: A Double-Blind, Placebo-Controlled Pilot Study in Breast Reduction Patients. Plast Reconstr Surg.

28. Strauch, B., Herman, C., Dabb, R., Ignarro, L.J., and Pilla, A.A. (2009). Evidence-based use of pulsed electromagnetic field therapy in clinical plastic surgery. Aesthet Surg J *29*, 135-143.

29. Li, Q., Kao, H., Matros, E., Peng, C., Murphy, G.F., and Guo, L. (2011). Pulsed Radio Frequency Energy (PRFE) Accelerates Wound Healing In Diabetic Mice. Plast Reconstr Surg.

30. Moffett, J., Griffin, N., Ritz, M., and George, F. (2010). Pulsed radio frequency energy field treatment of cells in culture results in increased expression of genes involved in the inflammation phase of lower extremity diabetic wound healing. The Journal of Diabetic Foot Complications *2*, 57-64.

31. Williamson, A., and Hoggart, B. (2005). Pain: a review of three commonly used pain rating scales. J Clin Nurs *14*, 798-804.

32. White, P.F., and Kehlet, H. (2010). Improving postoperative pain management: what are the unresolved issues? Anesthesiology *112*, 220-225.

33. Gilron, I., Orr, E., Tu, D., Mercer, C.D., and Bond, D. (2009). A randomized, double-blind, controlled trial of perioperative administration of gabapentin, meloxicam and their combination for spontaneous and movement-evoked pain after ambulatory laparoscopic cholecystectomy. Anesth Analg *108*, 623-630.

34. White, P.F., Sacan, O., Tufanogullari, B., Eng, M., Nuangchamnong, N., and Ogunnaike, B. (2007). Effect of short-term postoperative celecoxib administration on patient outcome after outpatient laparoscopic surgery. Can J Anaesth *54*, 342-348.

35. Bentall, R.H.C. (1981a). Effect of a 15 Watt Pulsed 27.12 MHz and a 2mW pulsed 3 MHz device on the tensile strength of rat abdominal wounds. In Proceedings of the 1st annual meeting of the Bioelectrial Repair and Growth Society. (Philadelphia, USA), p. p21.

Pulsed Radio Frequency Electromagnetic Field Therapy: A Potential Novel Treatment for Plantar Fasciitis

Joel Brook[1] DPM, Damien M. Dauphinee[2] DPM, Jaryl Korpinen[3] DPM, Ian M Rawe[4], PhD

1. Joel W. Brook, DPM, FACFAS. Dallas Podiatry Works, TX. Education Diector, Podiatric Surgery Residency Program, Hunts Regional Medical Center, Greenville TX
2. Complete Foot and Ankle Care of North Texas, PA, Denton, TX
3. Premier Foot & Ankle, Plano, TX
4. BioElectronics Corporation, Frederick, MD

Corresponding Author:
Ian M Rawe Ph.D
BioElectronics Corp.
4539 Metropolitan Ct.
Frederick, MD 21704
781-325-2439
301-874-6935 Fax
Email irawe@bielcorp.com

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Plantar fasciitis is a common cause of heel pain, while treatments are usually conservative they can take up to two years to achieve resolution. A double blind, multicenter, randomized, placebo controlled study was used to evaluate a small, wearable, extended use pulsed radio frequency electromagnetic field (PRFE) device as a treatment for plantar fasciitis. Seventy subjects diagnosed with plantar fasciitis were enrolled in the study. Subjects were randomly assigned a placebo or active PRFE device. The subjects were instructed to wear the PRFE device overnight and record morning and evening pain using a 0-10 point visual analogue scale (VAS), and log medication use. The primary outcome measure for the study was morning pain, a hallmark of plantar fasciitis. The study group using the active PRFE devices showed progressive decline in morning pain. The day 7 AM-VAS score was 40% lower than the day 1 AM-VAS score. The control group, in comparison, showed a 7% decline. There was a demonstrated significant different decline between the two groups (p=0.03). The PM-VAS scores declined by 30% in the study group and 19% in control group, though the difference was not significant. Medication in the study group also trended down, while the use in the control group remained consistent with day 1 levels. PRFE therapy worn on a nightly basis appears to offer a simple drug free, non-invasive therapy to reduce the pain associated with plantar fasciitis.

Key Words: Plantar, Fasciitis, Radiofrequency, Electromagnetic, Pain

Introduction

The plantar fascia is a thick fibrous band of connective tissue originating on the bottom surface of the calcaneus (heel bone) and extending along the sole of the foot towards the five toes. It acts to support the arch of the foot and aids in re-supination of the foot during propulsion (1). The condition plantar fasciitis is the most common cause of heel pain and estimates indicate that 1 million physician visits per year involve the diagnosis and treatment of plantar fasciitis (2). In addition, it is a common complaint in athletes resulting in approximately 8% of all running related injuries (3, 4).

The pain from plantar fasciitis is usually felt in the heel of the foot and is usually most acute during the first steps in the morning because the fascia tightens up during the night while sleeping. As the tissue warms pain subsides, but can return with activity and long periods of standing. The underlying condition is a degenerative condition, caused by microscopic tears in the collagen of the fascia. The condition has a detrimental impact on the quality of life and while conservative treatments are often effective the time to resolution can be up to 2 years however most patients see improvement by 9 months (5). Conservative therapies include rest, nonsteroidal anti-inflammatory medication, night splints, foot orthotics(6), stretching protocols (7) of the plantar fascia and gastrocnemius/soleues muscle(8). For persistent plantar heel pain extracorporeal shock wave therapy has been used but with mixed success. Surgery is sometimes employed as a last resort but there are complications that can arise and it is not always successful (9).

Pulsed radio frequency electromagnetic field therapy (PRFE), or pulsed electromagnetic field (PEMF) therapy has a long history in treating medical conditions. In 1947 the Federal Communications Commission assigned three frequencies at the short end of the RF band for medical use (40.68 MHz, 13.56 MHz and 27.12 MHz) (10).The frequency of 27.12 MHz is the most widely used in clinical practice. The first PRFE device, the Diapluse (Daipulse Corporation, Great Neck, NY) was commercially available in the 1950's, and was followed by other commercially available machines. PRFE is a non-invasive therapy that delivers electromagnetic energy into soft tissue generating an electric field which is thought to mediate the therapeutic effects (11). Many studies have shown the clinical efficacy and safety of PRFE therapy recently reviewed by Guo et al (12). For soft tissue injury these include ankle inversion treatment, where studies showed a reduction in pain and swelling (13, 14). PRFE therapy has shown to be beneficial in the treatment of neck pain (10, 15). The treatment of osteoarthritis with PRFE has been reported to improve joint mobility and decrease pain and stiffness (16-18). Recently there has been a focus on PRFE therapy and its application in controlling postoperative pain and in promoting the healing of chronic wounds. Significant decreases in postoperative pain have been reported after breast augmentation (19, 20) and breast reduction surgery (21), with a corresponding decreased need for narcotic pain medication during recovery. Healing of chronic wounds has also been reported in a number of case reports (22-26) and a retrospective study of a wound registry showed that PRFE holds promise to effectively promote the healing of chronic wounds (27). Significantly, studies on an animal models of Achilles tendon repair showed increased tensile strength and collagen alignment (28, 29) after PRFE treatment. After transection of the rat Achilles tendon, at 3 weeks tensile strength was increased by 69% compared with non-treated control animals (29), and in a model of Achilles tendonitis increased collagen alignment, decreased inflammation and better tissue normality was seen (28). And in vitro cuts in primary human tenocytes cultures from supraspinatus and quadriceps tendons exposed to electromagnetic field stimulation showed significantly accelerated cut closure 12 and 24 hrs after the injury (30).

Classically, most studies using PRFE have employed large, fixed mains powered devices, where therapy is delivered in the clinic. In this exploratory study for the treatment of plantar fasciitis the authors used an innovative, small wearable PRFE device (ActiPatch^{Tm}, BioElectronics Corp. Frederick, MD) which is used for extended periods, in this case as a home based therapy delivered nightly while sleeping.

Methods

The study is a multicenter, prospective randomized double-blind, placebo- and positive-controlled trial to determine the effects of nightly use of a wearable PRFE device (ActiPatch[Tm], Bioelectronics Corporation, Frederick MD). The study was approved by North Texas Institutional Review Board at Medical City Dallas, consent forms were obtained from the study participants and all rights of the enrolled subjects in the study were protected. The primary outcome measure for the study was morning pain, selected as morning pain is the hallmark of plantar fasciitis. Subjects who had been diagnosed plantar fasciitis were recruited from the clinical practices of the podiatrist authors. The primary diagnostic criteria was defined as the presence of tenderness at the insertion of the plantar fascia into the heel bone, either plantarmedially or plantarly. Radiography was used in all cases to rule out osseous causes of heel pain including stress fracture or bone tumor. Although patients with fat pad atrophy were not excluded, those with pain directly under the osseus prominance of the calcaneal tuber rather than at the insertion of the plantar fascia, were excluded. Patients in whom neuritis was determined to be the primary cause of heel pain as determined by palpation or percussion of the branches of the medial and lateral calcaneal nerves were excluded. Each subject recruited into the study randomly selected a coded PRFE device. The device used in this study was a pulsed radio frequency energy device ActiPatch, which emits a safe form of non-ionizing electromagnetic radiation. The carrier frequency is 27.12 MHz, the assigned FCC medical frequency, and has a pulse rate of 1000 pulses per second and 100 microsecond burst width. Peak burst output power of the 12 cm antenna is approximately 0.0098 watts covering a surface area of approximate 103 cm^2. The circuitry consists of low voltage (3 V) digital/analog electronics that control all timing functions to produce the therapeutic RF field, where the antenna field is placed directly above the therapeutic site. This closed loop system of the antenna, low energy signal generator circuit, and battery power supply, transfers the RF energy to the tissue. Placebo devices do not emit a radio frequency electromagnetic field but are identical to active devices including a LED light showing operation. The energy from the active device is not felt by the user and the active device cannot be distinguished in any way from the placebo device. Subjects were trained in the use of the PRFE devices which were worn nightly for 7 days with the antennae placed over the heel, the site of pain. The devices were kept in place with a wrap, and switched off when not in use. No other new treatments were started during the study. Subjects were asked to record their pain levels using a 0 -10 visual analogue scale (VAS). VAS scores were recorded both in the AM, assessed on the first steps after awakening, and the PM, at night before bed for the seven days of the study. Medication use was also recorded, medication use was left to the choice of each patient in the study.

Data Analysis:

After completion of the study and collection of all available data, the data was analyzed using EXCEL 2007 with QI macros (Denver, CO,). ANOVA was performed using a generalized linear model (GLM), a flexible generalization of ordinary linear regression using SAS software (Cary, NC).GLM generalizes linear regression by allowing the linear model to be related to the response variable via a link function and by allowing the magnitude of the variance of each measurement to be a function of its predicted value. The slope or rate of decline was compared using repeated measure analysis which allows for the comparison of the mean variables with time. This analysis allows for a statistical comparison between the rate of decline in the control and study groups. The slope is considered significantly different at the 95% confidence level. Trends in VAS scores were analyzed using the Friedman test for non-parametric repeated measures. Base rates for each group were done relative to the first VAS score taken in the morning of day 1.

While not a typically used methodology, to show the group trends in medication use over the 7 days of the study, the following method was used. Medications were converted to 1 pill doses using a base dose for each medication used by the study participants. One pill was recoded as either 200 mg ibuprofen, 250 mg acetaminophen, 250 mg naproxen, or 100 mg celecoxib. Use of a diclofenac topical patch was recorded as 1 dose.

Results

The planned enrollment for the study 140 patients and 70 active and 70 placebo coded devices were mixed in boxes. Patients randomly chose a device and the device code recorded. The planned enrollment was not met, due to time constraints, and only 70 patients were enrolled in the study of which 42 were active and 28 placebo. Given the shortness of the study and the simplicity of the treatment no patients were lost to follow up and there was no missing data. Though this was a multicenter study, inter site analysis was not performed as subject site recruitment data was not recorded by the study coordinator.

Demographic data indicated the randomization was successful (Table 1.). There was no significant difference in the age, height, weight and duration of plantar fasciitis between the two groups. The percent of females in the two groups was 75% control group and 73.8% study group.

Table 1. Demographic Data. The demographics of the two study groups are shown as means and standard deviation. There was no significant difference (P ≤ 0.05) detected in the demographic data of the two study groups.

	Control group	Study group	Significance p =
Age (years)	49.7 ±15.2	53.2 ±14.7	0.35
Height (inches)	64.3 ±2.9	65.5 ±3.0	0.09
Weight (lbs)	196.4 ±58.6	176.0 ±28.8	0.14
Duration of plantar fasciitis(months)	13.1 ±8.7	11.9 ±8.1	0.60

The PRFE therapy devices were well tolerated by all the patients and there were no adverse effects noted. Data was obtained from 70 enrolled patients and was available for statistical analysis. The mean AM-VAS scores along with standard deviation for the seven days of the study are presented (Table 2).

Table 2. The mean AM-VAS scores. The mean AM-VAS scores and standard deviations for the 7 days of the study. Friedman test for nonparametric repeated measures shows a significant difference (p = 0.036) between the means of the control and study groups.

Day	Control	Study
1	3.67 ± 2.01	4.38 ± 2.39
2	3.75 ± 2.30	3.64 ± 2.15
3	3.28 ± 2.40	3.45 ± 2.11
4	3.13 ± 2.37	3.26 ± 1.91
5	3.54 ± 2.86	2.87 ± 2.16
6	3.30 ± 2.59	3.01 ± 2.13
7	3.41 ± 2.80	2.64 ± 1.88

The day 1 VAS score were not significantly different between the study and control groups. The VAS pain scores for the 7 days of the study showed a consistency in the control group with a

day 1 to day 7 difference of 0.26 VAS points. In contrast the AM-VAS in the study group showed a steady decline. . The day 1 to day 7 VAS score difference was 1.74 VAS points, showing a 7.5 fold greater reduction in pain than the Placebo group (Figure 1).

Figure 1. The effect of overnight use of the ActiPatch device on morning pain. Data are presented as the mean reduction in AM VAS pain from day 1 to day 7. As can be clearly seen the level of pain decrease in the treated group was higher than that of the control group by a factor of 7.5.
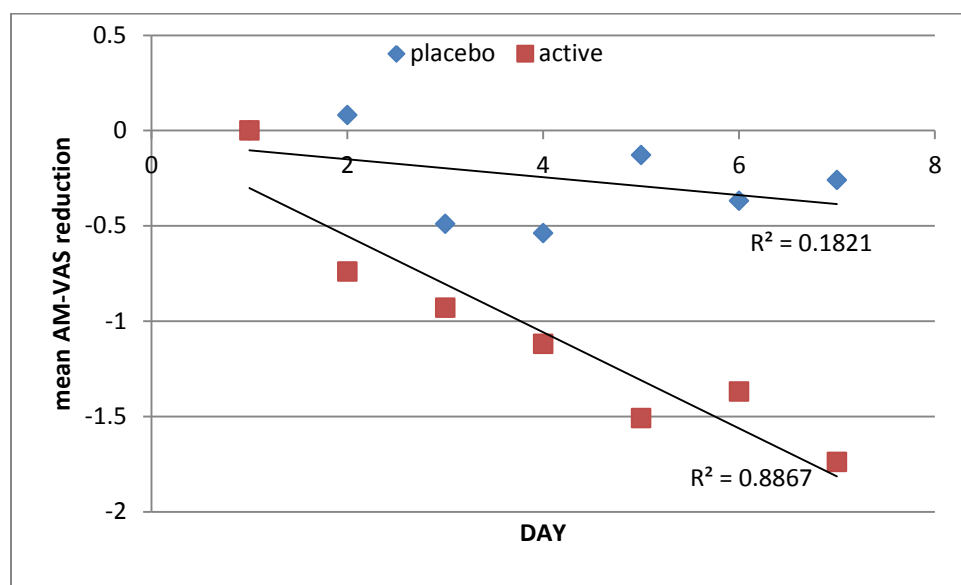
Regression analysis of the study group showed an $R^2 = 0.887$, with a p value of 0.002 and a slope of -0.252, i.e., y = 4.33 -0.252*day. For the control group the authors find $R^2 = 0.239$, with a p value of 0.265 and a slope of -0.051 i.e., y = 3.643 -0.051*day. The regression shows a significant downward slope of 0.25 VAS points per day in the study group. A standard repeated measure analysis using SAS's GLM routine showed that there is significantly different rates of improvement of morning pain between the two groups (p = 0.03). An F-test was also performed using EXCEL 2007 QI macros which showed the group means to be significantly different, p = 0.036.

The AM-VAS scores from day 2 through day 7 were compared to the day 1 groups AM-VAS score using a student t-test (Table 3). The AM-VAS scores through day 2 to day 7 in the control group show no significant differences compared to day 1. In contrast the steady decline in pain scores in the study group become significantly different at day 4 (p = 0.021) when compared to the day 1 score. The decline in pain continues to be significant through day 7.

Table 3. AM-VAS scores on day 2 through day 7 were compared to the respective day 1 AM-VAS score using a student t-test. Overnight wear of the Active device showed a significant decrease (p ≤ 0.05) at day 4 in the study group, but not in the control group.

Day		2	3	4	5	6	7
Study group	p-value	0.15	0.06	*0.021*	*0.0035*	*0.0076*	*0.00045*
Control group	p-value	0.90	0.52	0.36	0.83	0.61	0.69

The mean PM-VAS score with standard deviations are shown (Table 4). The control group and the study group showed declines when compared to the day 1 VAS score.

Table 4. The mean daily PM-VAS scores. The mean PM-VAS scores with standard deviation, along with day to day decline during the 7 day study period.

day	control	control day to day decline	study	study day to day decline
1	5.46 ±2.7	-	4.97 ±2.5	-
2	4.82 ±2.9	-0.64	4.64 ±2.5	-0.33
3	4.46 ±2.9	-0.36	4.25 ±2.7	-0.39
4	4.59 ±3.1	+0.13	3.74 ±2.2	-0.51
5	4.45 ±3.0	-0.14	3.81 ±2.4	+0.06
6	4.14 ±2.8	-0.31	3.79 ±2.5	-0.02
7	4.41 ±2.9	+0.33	3.48 ±2.4	-0.31
		-1.05		-1.49

The decline in the control group was 1.05 VAS points or 19%, whereas the decline in the study group was 1.49 VAS points or 30%. SAS ANOVA analysis and F-test showed no significant difference between the groups. However, the decline in the control group from day 1 to day 2 was 0.64 VAS points and a further 0.36 VAS points from day 2 to day 3. From day 3 to day 7 there was no further decline in the mean VAS score, 4.46 and 4.41points respectively. In contrast the VAS decline was more evenly spread in the study group. With the day 1 to day 2 decline 0.33 VAS points, and day 2 to day 3 decline 0.39 points. The VAS point decline from day 3 to day 7 was 0.77 VAS points in the study group. Figure 2A shows the mean decline on PM-VAS of both groups during the 7 days of the study, and Figure 2B shows the day 3 -7 mean decline.

Figure 2A The mean PM-VAS point reduction after overnight use of the Actipatch device. Data are presented as the mean reduction in PM-VAS pain from day 1 to day 7, there is no significant difference between the two groups. The study group decreased 1.49 VAS points compared to 1.05 VAS points in the control group.
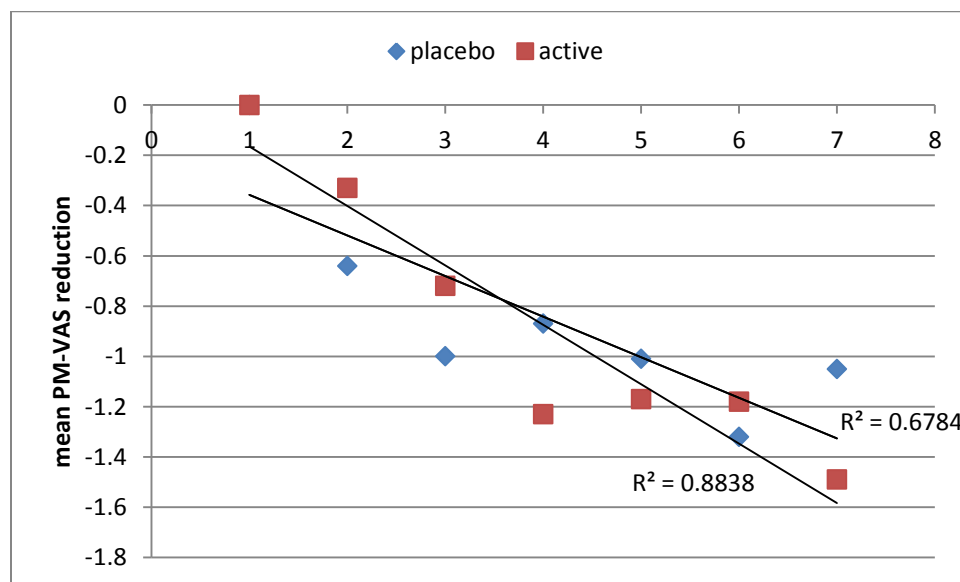
Figure 2B. The mean PM-VAS score reduction from day 3 to day 7. The data shows that the control group mean PM-VAS score remains essentially unchanged from day 3 through to day 7, while the study group mean PM-VAS shows a continued decline.
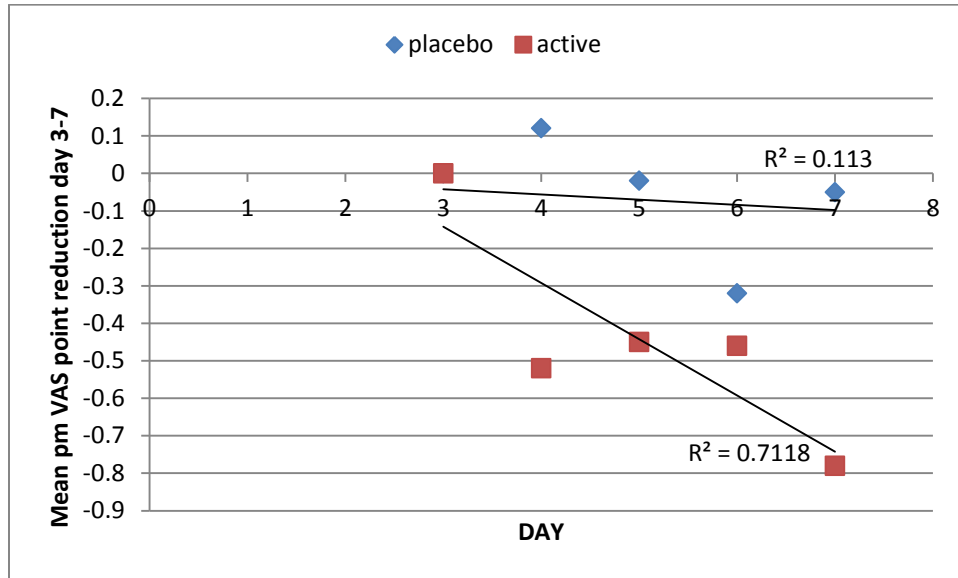
Similar to the results of the AM-VAS analysis when comparing the PM-VAS scores of day 2 through day 7 to the respective day 1 PM-VAS using a student t-test. Significance was shown at ay 4 through day 7 in the study group, there was no significance decrease in the control group (Table 5).

Table 5. The day 1 PM-VAS scores were compared against the mean PM-VAS for the days 2-6 using a students t-test. Significance ($p \leq 0.05$) was seen at day 4 through day 7 in the study group only.

Day		2	3	4	5	6	7
Study Group	P value	0.55	0.21	*0.02*	*0.03*	*0.03*	*0.007*
Control Group	P value	0.41	0.20	0.28	0.20	0.08	0.17

Medication

The medication used by each group is shown (Table 6). While the randomization of the study was shown to be successful, determined by the demographic data (Table 1), a higher percent of patients were taking medication in the control group (9/28 or 32.1%) compared to the study group (10/42 or 23.8%) on day 1. However, of those patients in both study groups taking medication, the average pill use on day one was very similar, control group 2.55, and study group 2.44 pills per subject (Table 7). This is also shown by the total pill use, which was similar at day 1, study group 22 and control group 23. The daily total pill use, and average patient pill use in the control showed day to day variability but overall showed no decline. Whereas in the study group the total pill, and patient average use trended down (Table 7, Figure 3.).
Figure 3. The mean daily pill for the study and control groups. There is decline of pill use in the study group 22 pills on day 1 to 11 pills in on day 7, in contrast there is no decline in pill use in the control group, 23 pills day 1 and 28 pills day 7.
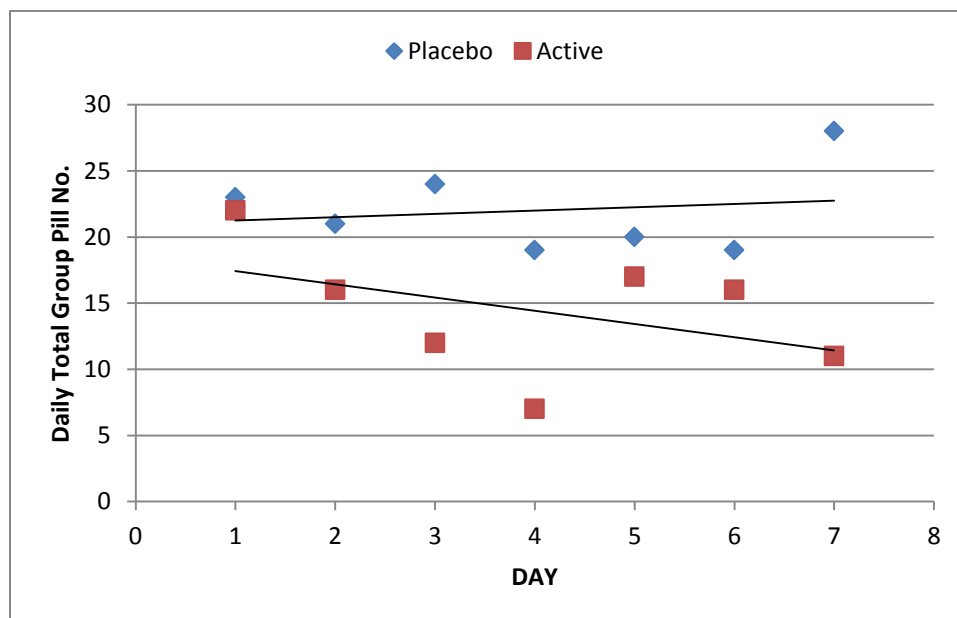
By day 7 the pill use in the control group was 28 and in the study group 11. And the average pill use was 2.8 pills per patient in the control group, and 1.57 pills per patient in the study group. The number of patients taking pills in the control was 10/28 or 35.7% and in the study group 7/42 16.6% at day 7. However there was no significant difference determined between the two groups.

Table 6. Group medication use. The total and type of pain medications used by each group in the study are shown. The control group used 154 pain medication pills compared to 101 pain medication pills in the study group. (1 pill is counted as either 200mg ibuprofen, 250mg acetaminophen, 250 mg naproxen, 100 mg celebrex, 1 fletchor patch).

Medication	control	study
acetaminophen 250mg	3	24
ibuprofen 200mg	85	46
naproxen 250mg	38	22
celebrex	28	0
flector patch (diclofenac)	0	7
loratab	0	2
Total	154	101

Table 7. Medication use. The number of subjects using medication, the total pill use, and the average subject pill use in the control and study groups by day.

Day	1	2	3	4	5	6	7
control group-subject No. using Meds	9	8	10	8	9	8	10
control group-total Med use	23	21	24	19	20	19	28
control group-subject Med average pill use	2.55	2.65	2.4	2.37	2.22	2.37	2.80
study group-subject No. using Meds	9	7	7	5	7	8	7
study group-total Med use	22	16	12	7	17	16	11
study group -subject Med average pill use	2.44	2.28	1.71	1.4	2.42	2.0	1.57

Discussion

In this study we have presented results from a prospective study using a small, lightweight wearable PRFE device as a treatment for plantar fasciitis. Subjects were instructed to wear the device overnight, and pain in the AM and PM was recorded for 7 days. The results showed that overnight wear of the PRFE device was effective at significantly reducing morning pain, a hall mark of plantar fasciitis. The significant decline in morning pain in the study group wearing the active PRFE device was 40%, compared to the 7.9% in the control group over the 7 day study period. The analysis of the PM pain showed no significant difference between the two groups. The study group declined 30% and the control group 19%. It should be noted that the control group had a day 1 to day 3 decline of 1.00 VAS points in the pm, although very little decline, (0.05 VAS points) was seen for the following days 3 -7. This suggests that there was a strong initial placebo effect, for the first few days of the study. The decline in the study group was more consistent, indicating a longer study period would have resulted in a significance difference between the two groups. Medication use in the study group trended down during the 7 day study while remained more consistent in the control group, though the results were not significantly different. Consistent decreases in morning pain seen in the study group would be expected to lead to decreased medication use, which was seen.

The PRFE device used in this study is based on work pioneered by Dr Bentall in the 1980's who first showed that reducing power and size but extending use time produces equivalent results to larger more powerful devices (31). A study by Nicolle and Bentall on surgical recovery showed that extended use PRFE devices were able to control edema following blephoraplasty. There has been a new focus on small extended use PRFE devices and a number of publications on postoperative recovery and wound healing have been published(19-21, 26).

The current treatment for a majority plantar fasciitis cases result in a positive resolution with conservative modalities (6, 32-35). Conservative forms of treatment, including nonsteroidal anti-inflammatory drugs (NSAIDs), heel pads or orthotics, physical therapy, stretching of the gastrocnemius-soleus and corticosteroid injections, provide substantial relief for about 80% of patients. However, along with the long time to resolution there are further drawbacks to some of these treatments. Injection of corticosteroids for the treatment of plantar fasciitis is almost always painful and can course both local and systemic side effects (36). Long term use of NSAIDs can have significant side effects such as gastrointestinal complications and increased risk of serious cardiovascular events (37). While custom orthotics are often prescribed they may only show a short term benefit in reducing the pain associated with plantar fasciitis (38).

On the failure of conservative therapies treatments such as extracorporeal shock wave therapy and surgery are used. Extracorporeal shock wave therapy has been reported to be effective in some studies where conservative treatments have failed. Metzner et al (39) reported good results with extracorporeal shockwave therapy. In this study success was defined as a 30% VAS reduction which was seen in 81% of patients at 6-week follow up. However, other studies report conflicting results with the treatment being seen as no better than sham therapy (40-42). Though surgery to treat plantar fasciitis is used as a last resort, it has variable (70–90%) success rate, and recovery from surgery can vary from several weeks to few months. Potential complications include transient swelling of the heel, heel hyposthesia, rupture of plantar fascia, flattening of the longitudinal arch, and calcaneal fracture (9).

This is the first study to show that PRFE therapy used in this format can potentially treat plantar fasciitis. PRFE therapy for plantar fasciitis appears to offer a therapy that is easy to use,

non-invasive, drug free and with no reported side effects. The results from this initial study indicate that PRFE therapy results in a relatively rapid decline of pain given the usually protracted nature of the condition.   However, there are a number of limitations with this study, including the length of time that data was collected (7 days), the lack of long term follow up and inter-center analysis. Also, no power analysis was performed to calculate study size, due to the lack of data on the effects of this form of therapy on plantar fasciitis heel pain. Sample size was determined by the time podiatric authors allotted to do the study, which resulted in the lower than anticipated recruitment goals. None the less, the study results suggest that PRFE therapy is this form holds promise as a new treatment of plantar fasciitis.

This is the first study utilizing this form of therapy for plantar fasciitis heel pain. The results from the study indicate that further studies are warranted to confirm these initial finding.

References

1. Michaud T, C. (1997) Foot Orthoses and Other Forms of Conservative Foot Care, (Massachusetts:, Ed.), Lippincott, Williams & Wilkins.
2. Riddle DL, and Schappert SM. Volume of ambulatory care visits and patterns of care for patients diagnosed with plantar fasciitis: a national study of medical doctors. Foot Ankle Int 25:303-310, 2004.
3. Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, and Zumbo BD. A retrospective case-control analysis of 2002 running injuries. Br J Sports Med 36:95-101, 2002.
4. Lysholm J, and Wiklander J. Injuries in runners. Am J Sports Med 15:168-171, 1987.
5. Urovitz EP, Birk-Urovitz A, and Birk-Urovitz E. Endoscopic plantar fasciotomy in the treatment of chronic heel pain. Can J Surg 51:281-283, 2008.
6. Lynch DM, Goforth WP, Martin JE, Odom RD, Preece CK, and Kotter MW. Conservative treatment of plantar fasciitis. A prospective study. J Am Podiatr Med Assoc 88:375-380, 1998.
7. Glazer JL. An approach to the diagnosis and treatment of plantar fasciitis. Phys Sportsmed 37:74-79, 2009.
8. Barry LD, Barry AN, and Chen Y. A retrospective study of standing gastrocnemius-soleus stretching versus night splinting in the treatment of plantar fasciitis. J Foot Ankle Surg 41:221-227, 2002.
9. Young CC, Rutherford DS, and Niedfeldt MW. Treatment of plantar fasciitis. Am Fam Physician 63:467-474, 477-468, 2001.
10. Foley-Nolan D, Barry C, Coughlan RJ, O'Connor P, and Roden D. Pulsed high frequency (27MHz) electromagnetic therapy for persistent neck pain. A double blind, placebo-controlled study of 20 patients. Orthopedics 13:445-451, 1990.
11. Kloth LC, and Pilla AA. Electromagnetic stimulation for wound repair., In Wound Healing: Evidence-Based Management, pp 514-544, F. A. Davis Company, Philadelphia. (2010)
12. Guo L, Kubat NJ, and Isenberg RA. Pulsed radio frequency energy (PRFE) use in human medical applications. Electromagn Biol Med 30:21-45, 2011.
13. Pennington GM, Danley DL, Sumko MH, Bucknell A, and Nelson JH. Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. Mil Med 158:101-104, 1993.
14. Wilson DH. Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. Physiotherapy 60:309-310, 1974.
15. Foley-Nolan D, Moore K, Codd M, Barry C, O'Connor P, and Coughlan RJ. Low energy high frequency pulsed electromagnetic therapy for acute whiplash injuries. A double blind randomized controlled study. Scand J Rehabil Med 24:51-59, 1992.
16. Laufer Y, Zilberman R, Porat R, and Nahir AM. Effect of pulsed short-wave diathermy on pain and function of subjects with osteoarthritis of the knee: a placebo-controlled double-blind clinical trial. Clin Rehabil 19:255-263, 2005.
17. Jan MH, Chai HM, Wang CL, Lin YF, and Tsai LY. Effects of repetitive shortwave diathermy for reducing synovitis in patients with knee osteoarthritis: an ultrasonographic study. Phys Ther 86:236-244, 2006.
18. Callaghan MJ, Whittaker PE, Grimes S, and Smith L. An evaluation of pulsed shortwave on knee osteoarthritis using radioleucoscintigraphy: a randomised, double blind, controlled trial. Joint Bone Spine 72:150-155, 2005.
19. Rawe IM, Lowenstein A, Barcelo CR, and Genecov DG. Conrol of postoperative pain with a wearable continuously operating pulsed radio frequency energy device - A preliminary study. Aesthetic Plast Surg inpress, 2011.

20. Heden P, and Pilla AA. Effects of pulsed electromagnetic fields on postoperative pain: a double-blind randomized pilot study in breast augmentation patients. Aesthetic Plast Surg 32:660-666, 2008.
21. Rohde C, Chiang A, Adipoju O, Casper D, and Pilla AA. Effects of pulsed electromagnetic fields on interleukin-1 beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients. Plast Reconstr Surg 125:1620-1629, 2010.
22. Fletcher S. Successful treatment of venous stasis ulcers with combination compression therapy and pulsed radio frequency energy in a patient scheduled for amputation. J Wound Ostomy Continence Nurs 38:91-94, 2011.
23. Frykberg R, Martin E, Tallis A, and Tierney E. A case history of multimodal therapy in healing a complicated diabetic foot wound: negative pressure, dermal replacement and pulsed radio frequency energy therapies. Int Wound J 8:132-139, 2011.
24. Larsen JA, and Overstreet J. Pulsed radio frequency energy in the treatment of complex diabetic foot wounds: two cases. J Wound Ostomy Continence Nurs 35:523-527, 2008.
25. Maier C, Kibbel K, Mercker S, and Wulf H. [Postoperative pain therapy at general nursing stations. An analysis of eight year's experience at an anesthesiological acute pain service]. Anaesthesist 43:385-397, 1994.
26. Rawe IM, and Vlahovic TC. The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: A case report. Int Wound J, 2011.
27. Frykberg RG, Driver VR, Lavery LA, Armstrong DG, and Isenberg RA. The Use of Pulsed Radio Frequency Energy Therapy in Treating Lower Extremity Wounds: Results of a Retrospective Study of a Wound Registry. Ostomy Wound Manage 57:22-29, 2011.
28. Lee EW, Maffulli N, Li CK, and Chan KM. Pulsed magnetic and electromagnetic fields in experimental achilles tendonitis in the rat: a prospective randomized study. Arch Phys Med Rehabil 78:399-404, 1997.
29. Strauch B, Patel MK, Rosen DJ, Mahadevia S, Brindzei N, and Pilla AA. Pulsed magnetic field therapy increases tensile strength in a rat Achilles' tendon repair model. J Hand Surg Am 31:1131-1135, 2006.
30. Denaro V, Ruzzini L, Barnaba SA, Longo UG, Campi S, Maffulli N, and Sgambato A. Effect of pulsed electromagnetic fields on human tenocyte cultures from supraspinatus and quadriceps tendons. Am J Phys Med Rehabil 90:119-127, 2011.
31. Bentall RHC. Low-level pulsed radiofrequency feilds and the treatment of soft-tissue injuries. Bioelectrochemistry and Bioenergetics 16:531-548, 1986.
32. DiGiovanni BF, Nawoczenski DA, Lintal ME, Moore EA, Murray JC, Wilding GE, and Baumhauer JF. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain. A prospective, randomized study. J Bone Joint Surg Am 85-A:1270-1277, 2003.
33. Pfeffer G, Bacchetti P, Deland J, Lewis A, Anderson R, Davis W, Alvarez R, Brodsky J, Cooper P, Frey C, Herrick R, Myerson M, Sammarco J, Janecki C, Ross S, Bowman M, and Smith R. Comparison of custom and prefabricated orthoses in the initial treatment of proximal plantar fasciitis. Foot Ankle Int 20:214-221, 1999.
34. Buchbinder R. Clinical practice. Plantar fasciitis. N Engl J Med 350:2159-2166, 2004.
35. Landorf KB, Keenan AM, and Herbert RD. Effectiveness of different types of foot orthoses for the treatment of plantar fasciitis. J Am Podiatr Med Assoc 94:542-549, 2004.
36. Brinks A, Koes BW, Volkers AC, Verhaar JA, and Bierma-Zeinstra SM. Adverse effects of extra-articular corticosteroid injections: a systematic review. BMC Musculoskelet Disord 11:206, 2010.

37.	Peterson K, McDonagh M, Thakurta S, Dana T, Roberts C, Chou R, and Helfand M. In Drug Class Review: Nonsteroidal Antiinflammatory Drugs (NSAIDs): Final Update 4 Report, Portland (OR). (2010)
38.	Landorf KB, Keenan AM, and Herbert RD. Effectiveness of foot orthoses to treat plantar fasciitis: a randomized trial. Arch Intern Med 166:1305-1310, 2006.
39.	Metzner G, Dohnalek C, and Aigner E. High-energy Extracorporeal Shock-Wave Therapy (ESWT) for the treatment of chronic plantar fasciitis. Foot Ankle Int 31:790-796, 2010.
40.	Haake M, Buch M, Schoellner C, Goebel F, Vogel M, Mueller I, Hausdorf J, Zamzow K, Schade-Brittinger C, and Mueller HH. Extracorporeal shock wave therapy for plantar fasciitis: randomised controlled multicentre trial. Bmj 327:75, 2003.
41.	Speed CA, Nichols D, Wies J, Humphreys H, Richards C, Burnet S, and Hazleman BL. Extracorporeal shock wave therapy for plantar fasciitis. A double blind randomised controlled trial. J Orthop Res 21:937-940, 2003.
42.	Buchbinder R, Ptasznik R, Gordon J, Buchanan J, Prabaharan V, and Forbes A. Ultrasound-guided extracorporeal shock wave therapy for plantar fasciitis: a randomized controlled trial. Jama 288:1364-1372, 2002.

Indication: Pain and Inflammation

Pain and Inflammation of Delayed Onset Muscle Soreness

Use of ActiPatch Device for Treatment of Delayed Onset Muscle Soreness – Comparison to Acetaminophen and Control Group

Sheena Kong, M.D.

Introduction

Background

Delayed Onset Muscle Soreness (DOMS) is a condition associated with increased physical exertion. This condition is experienced by all individuals regardless of fitness level as it is a normal physiological response to increased exertion and the introduction of unfamiliar or strenuous physical activities. The pain caused by DOMS can impair physical training and performance, and as a result, it is of great concern to trainers, coaches, and therapists. DOMS affects many more individuals than just athletes. Many ordinary people are developing this condition as a result of excessive physical or out of the ordinary exertion. The pain and discomfort associated with this condition generally peaks at between 36 to 72 hours after an exercise routine and usually resolves within 96 hours.

For several decades DOMS had been attributed to lactic build up in the muscles after exertion. Over the past few years this assumption has been shown to be unrelated to this condition. Several research studies have indicated that lactate levels return to normal within 60 minutes post exercise. Therefore, increased lactate levels cannot cause DOMS.

DOMS is predominately caused by eccentric exercise. Connolly et al. (2003) explains that the injury that results from eccentric exercise causes damage to the muscle cell membrane, which sets off an inflammatory response. The inflammatory response leads to the formation of metabolic waste products, which act as chemical stimulus to the nerve endings that directly cause a sensation of pain and swelling.

W. Stauber et al (2000) used a high-powered microscope to analyze muscle fibers after an intense workout. Based on his research it was clear that cell membranes were ruptured and other structural components were disrupted; however, damage to the muscle fibers is relatively small. This damage is not limited to one area but occurs throughout the muscle fiber. This microscopic muscle damage causes an inflammatory response. It is this inflammatory response that causes muscle soreness due to: 1) the accumulation of fluid (swelling) and 2) chemicals secreted by white blood cells that activate pain receptors (Smith, 1991).

While there has been some research conducted on the treatment of DOMS, no particular treatment option has been proven to be dominant in treating or preventing the condition. The most popular intervention is pharmacological options using non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen. Stretching and warm-up exercises as well as nutritional augmentation via supplements have also been explored with varying degrees of success.

NSAIDs, such as aspirin and ibuprofen, and acetaminophen are popular treatments for DOMS, but some of the research conducted in this area is inconclusive. Additionally, there are significant concerns associated with negative potential side effects such as gastrointestinal distress, liver toxicity and related coronary issues.

There has been considerable research relative to using nutritional supplementation as a potential treatment for DOMS with particular emphasis on vitamins E and C and other antioxidants, which are thought to reduce the proliferation of free radicals generated during an inflammatory response. These effects are inconclusive as are other investigations into use of L-carnitine.

While neither NSAIDs nor nutritional supplements have been proven to reduce the onset of DOMS, there has been some research suggesting that simple warm-up exercises can meaningfully reduce the onset of the condition. Szymanski (2003) introduced the "repeated-bout effect" as a way to reduce DOMS. The repeated-bout is a progressive adaptation to exercise that has been shown to consistently reduce DOMS and exercise induced damage to muscles.

ActiPatch is a miniaturized medical device that delivers continuous electromagnetic therapy to restore damaged cells. The device is a Class III medical device that is available only through a licensed health care practitioner in the United States. The device, however, is widely available on an over-the-counter basis outside of the United States. Significant clinical data shows that ActiPatch reduces edema, inflammation and pain. ActiPatch uses a mild electrical current and radiofrequency waves at a frequency that stops the release of pain and inflammatory mediators, increasing blood flow, and reestablishing normal cell interaction.

Pulsed electromagnetic stimulation (PEMF) in some form has been used or investigated since the early 1930s. There is a large body of clinical experience that has realized its value as an effective treatment for tissue trauma, particularly in the early stages of inflammation. Numerous studies are available that document its effectiveness in orthopedic surgery, arthritis, and even plastic surgery (breast augmentation). While no study has demonstrated the complete elimination of pain, PEMF has shown less dependence on medications and some enhancement of the recovery period. Also, there has not been a single study showing any harmful effects so it is safe to conclude that PEMF is safe for human use.

The precise mechanism by which PEMF works on controlling pain after injury is not known. It is theorized that it may affect pain levels by its effect of nitric oxide (NO) release, a short-lived signaling molecule in the anti-inflammatory cascade. It is also suggested that it has an effect on stabilizing cell membranes such that the edema phase of an injury is more rapidly resolved.

ActiPatch devices function at a frequency in the 27.1 MHz ISM band and are confined within the field of the patch's loop antenna. The patch induces electric current in human tissue, but it is oscillating at such a high frequency that it cannot be detected by the patient. The high frequency results in a depth of penetration into the tissues of approximately 10 cm. When the patch is used over a 24 hour period, it produces an absorbed energy of 630 mJ/cc which is well within the range of effectiveness for soft tissue injuries. The patch produces a power density at the skin surface between 14 and 73 µW/cm² and induces an electrical field of about 10 milliVolt/cm, resulting in adsorbed power levels in the range of 7.3 µW/cm3. This provides field exposure levels at the target tissue that are five to nine orders of magnitude above the thresholds which have been established for non-thermal electromagnetically induced biological effects at the cell and tissue level.

The ActiPatch uses proven medical technology to truncate the human body's natural inflammatory response breaking the cycle of chronic inflammation. ActiPatch does this by delivering pulsed electromagnetic energy directly to the affected area and driving out the edematous fluid along with byproducts of the damaged tissue. The affect is a well-documented and a significant overall improvement in the restorative and recovery process following injury resulting in a substantial reduction in the pain associated with soft tissue injury. These statements are supported by multiple studies, but no specific research has been done relative to its effects on DOMS.

ActiPatch was cleared by FDA in 2002 for the treatment of edema following blepharoplasty. Clinical data presented by BioElectronics to Health Canada resulted in its approval for relief of pain in musculoskeletal complaints, and the product is now available over-the-counter throughout Canada. The product is also cleared for over-the-counter sales in European Union countries and other countries throughout the world.

Study Execution

Study Design

- This was an observational study to evaluate the treatment of delayed onset muscle soreness.
- Study participants were placed randomly into one of three groups 1) a control group, 2) a group that utilized ActiPatch, and 3) a group that received over-the-counter strength acetaminophen
- 102 participants in total - 38 used the ActiPatch, 38 acting as control, and 26 used acetaminophen
- Sample size for acetaminophen group was smaller due to resistance from participants to consume acetaminophen
- Age range from 18 to 35, subjects were healthy collegiate athletes and trainers who exercise regularly and participate in team sports
- Interventions were approximately 20 sets of 10 repetitions of bicep resistance exercises using free weights to induce DOMS in the bicep muscles of both arms

- Approximately 48 hours post exercise, participants returned to study site and were given a Pain Recording Scale (Visual Analogue Scale) sheet to record their perceived level of DOMS pain in their bicep muscles.

Exclusion Criteria

- Anyone who is unable to give consent or document written consent in English
- Anyone who is confirmed or who could possibly be pregnant
- Anyone with allergy or intolerance to acetaminophen
- Anyone with known active liver disease

Recruitment of Participants

Participants were recruited from collegiate athletic teams and athletic training personnel.

Randomization

After the DOMS inducing resistance exercise regiment was completed, each study participant was randomly assigned to one of the three participating groups. Study participants assembled randomly in a straight line. The number of participants in the line was divided by three. Starting left to right of the line the three groups were selected with the first third becoming the ActiPatch group, second third becoming the control group and the final third becoming the acetaminophen group.

Adverse Events Reporting

As described in the informed consent forms, all adverse events were to be reported to the investigating physician or the collegiate athletic training personnel. Participants were given the direct phone number to the principal investigator. No adverse events were reported to either the principal investigator for the collegiate athletic training personnel.

Data Collection

Measurements of DOMS-related muscle pain assessments were done by the participants who completed a simple form that recorded pain and muscle soreness levels on the VAS line. The data was collected by the athletic training personnel under

the supervision of the principal investigator. The principal investigator transferred the data to a spreadsheet from which statistical analysis was performed.

Statistical Analysis

Data was collected from the participants approximately 48 hours after the administration of the DOMS inducing resistance exercise regiment using a VAS (Visual Analogue Score) pain assessment.

Statistical Analysis

Data were collected at the end of the study. The monitor copied the data from the individual sheets and placed in a spreadsheet with one entry per participant depending on the participant's particular group, i.e., Tylenol, Control or ActiPatch. Thus there were three columns, one for each group. At the end of the study, the data were provided for analysis.

The data were analyzed using Excel macro's. Means, variances and standard deviations for the VAS scores were calculated for each subsample. The difference between cell means was tested using t-tests with the following formula:

$$t = \frac{\bar{X}_T - \bar{X}_C}{\sqrt{\dfrac{var_T}{n_T} + \dfrac{var_C}{n_C}}}$$

where X is the mean for the group, VAR is the variance of the observations, n is the sample size and the subscripts T and C represent the two different groups being compared, e.g. "treatment" and "control" group.

Acceptance Criteria

This study used two tailed tests and significance levels of .05, .025 and .001 to determine the significant differences in sample means.

Results

102 patients were enrolled in this study, 38 using the ActiPatch, 38 acting as control, and 26 using Tylenol. Table 1 shows the mean VAS scores for each subsample along with the variances for these means, i.e., var/n .

Table 1: Group Means and Variances

	Tylenol	Control	ActiPatch
Means	2.507	3.179	1.500
Means Variance	.1315	.1678	.0620

Table 2 presents the results of the individual t-tests. Comparisons were made between ActiPatch and the control group and ActiPatch and the Tylenol group. The former comparison was significant at the .001 level; the latter was significant at the .05 level.

Table 2: t-test statistics

	t-statistic	degrees of freedom	significance level
ActiPatch vs. Control	3.504	78	.001
ActiPatch vs. Tylenol	2.290	64	.05

Discussion

The data from this study demonstrates the ActiPatch device manufactured by BioElectronics Corporation had a significant effect on reducing DOMS-related symptoms of muscle pain and soreness when compared to both a control group that received no treatment and a group that was treated with 1 gram of acetaminophen in the form of Extra Strength Tylenol. Based on this data, the principal investigator concludes that ActiPatch is safe and effective treatment for DOMS.

The use of ActiPatch seems to be a convenient, safe and effective new treatment for muscle pain and soreness, especially when compared to currently FDA approved over the counter treatments, such as acetaminophen, NSAIDs and other pain medications that may have questionable safety profiles.

A Randomized, Double-Blind Study Evaluating the Safety and Efficacy of Allay Menstrual Pain Therapy in the Treatment of Primary Dysmenorrhea

Investigators: Barry L. Eppley, M.D., D.M.D. & Sheena Kong, M.D. (June 2009)

Prepared: June 2009

Revision History: September 2010

Study Title: A Randomized, Clinical Study Evaluating the Safety and Efficacy of Allay Menstrual Pain Therapy in the Treatment of Primary Dysmenorrhea

Name of Device Tested: Allay Menstrual Pain Therapy

Indication: Pain and Edema Resulting from Menstruation

Sponsor: BioElectronics Corporation

 4539 Metropolitan Court

 Frederick, MD 21704

Study Number: BIEL-002

Phase of Development: N/A

Study Start Date: 15 January 2009 (First Subject Enrolled)

Study End Date: 15 May 2009 (Last Subject Results Recorded)

Primary Investigators: Sheena Kong, M.D. & Barry Eppley, M.D., D.M.D.

Responsible Medical

Monitor: Barry Eppley, M.D., D.M.D.

Report Date: June 2009

_____

This study was conducted in accordance with the guidance of Good Clinical Practice (GCP), including archiving of essential documents.

Title	
A Randomized, Clinical Study Evaluating the Safety and Efficacy of Allay Menstrual Pain Therapy in the Treatment of Primary Dysmenorrhea	
Investigators	
Multicenter; refer to Appendix A for a complete listing of investigators and locations.	
Study Centers	
Two centers in the United States enrolled subjects in this clinical study. One center was located in San Francisco, CA, (SF) and the other in Indianapolis, IN (IN)	
Publications	
None	
Study Period	
15-Jan-09	
15-May-09	
Objective	
The objective of this study was to characterize the risks, effectiveness, and benefits of using Allay Menstrual Pain Therapy for the treatment of primary dysmennorhea.	
Methodology	
A prospective randomized double-blind, placebo- and positive-controlled study of Allay Menstrual Pain Therapy versus placebo in adult women for primary dysmenorrhea. The study was randomized in a 1:1 ratio at the time of enrollment to receive either an active Allay device or a placebo device.	
Number of Subjects (Planned and Analyzed)	
Planned: 70 Total Subjects, at least 30 Placebo, 30 Active	
Analyzed: 91 Indianapolis: 47 San Francisco: 44	
Diagnosis and Main Criteria for Inclusion	
Women ages 18-35 suffering from (self-diagnosed) moderate to severe pain and discomfort resulting from menstruation.	
Persons who do not have implanted medical devices (ie. cardiac pacemakers, implantable cardioverter defibrillators (ICD), neurostimulators, etc.).	
Persons who have not undergone abdominal surgery.	
Duration of Treatment	
One menstrual cycle (5-7 days), one month. Subjects were instructed to wear the device continuously for at five to seven consecutive days from the onset of their menstrual cycles. Subjects were also instructed to remove the device before coming into con	

STUDY SYNOPSIS (Continued)

Investigational Product, Dose and Mode of Administration	
ActiBand, Pulsed Electromagnetic Field Therapy (PEMF).	
Power Source: 3.5 V Battery; Carrier Frequency: 27.1 MHz; Pulse Width: 100 microseconds; Pulse Repetition Frequency: 1KHz	
Reference Therapy	
None	
Criteria for Evaluation:	
Efficacy: Self-reported levels of pain	
Safety: Safety and Tolerability	
Outcome Measures: Quality of life; Subjective (perceived) pain relief, Symptoms Questionnaire Data, Comment Card	
Statistical Methods:	
Control: Patients self-reported perceived levels of pain for each day of their menstrual cycle prior to participation in the clinical trial.	
Efficacy: Self-reported levels of pain during the trial were compared to the control, and statictics were collected on the percentages of pain reduction on a per-patient basis to normalize the data.	
Safety: Adverse events were assessed. The safety data summary includes all participants who wore the device at least one day.	
Outcome Measures: Quality of life, Adherence Questionnare Data, Treatment Satisfaction	

SUMMARY OF RESULTS

Introduction

Primary Dysmenorrhea, commonly referred to as menstrual cramping, is a medical condition characterized by pain from contractions in the lower abdomen occurring at the onset of menstruation in the absence of an identifiable pelvic disease. Sharp pains in the lower abdomen begin at the start of menstruation and may continue for up to 3 or 4 days. The pain can range from mild to severe and can often interfere with many normal activities. While the majority of women who have menstrual periods experience some discomfort, an estimated 10% or more are temporarily disabled by the high level of pain that they experience. It is distinguished from secondary dysmenorrhea, which refers to painful menses resulting from pelvic pathology such as endometriosis.

Many different treatment strategies have been tried for menstrual pain but the most commonly used are non-steroidal anti-inflammatory drugs. (NSAIDS) Despite drug therapy, universal relief is not obtained and some patients experience gastric upset and other minor problems with NSAID use.

Pulsed electromagnetic field (PEMF) therapy in some form has been used or investigated since the early 1930s. There is a large body of clinical experience that has realized its value as an effective treatment for tissue trauma, particularly in the early stages of inflammation. Numerous

studies are available that document its effectiveness in orthopedic surgery, arthritis, and even plastic surgery (breast augmentation, rhinoplasty, etc.). While no study has demonstrated the complete elimination of pain or need for some medication relief, PEMF has shown less dependence on medications and some enhancement of the recovery period. Also, no known studies have reported adverse or harmful effects so it is fair to conclude that PEMF is safe for human use.

The precise mechanism by which PEMF works on controlling pain after injury is not known. It is theorized that it may affect pain levels by its enhancement of nitric oxide (NO) release, a short-lived signaling molecule in the anti-inflammatory cascade. It is also suggested that it has an effect on stabilizing cell membranes such that the edema phase of an injury is less or more rapidly resolved.

Allay menstrual patches have been specifically developed for application over the uterine area. The looped design functions at a frequency in the 27.1 MHz ISM band and is confined within the field of the patch's loop antenna. The patch induces electric current in human tissue but is oscillating at such a high frequency that it cannot be detected by the patient. The high frequency results in a depth of penetration into the tissues of approximately 10 cm. When the patch is used over a 24 hour period, it produces an absorbed energy of 630mJ/cc, which is well within the range of effectiveness for soft tissue injuries. The patch produces a power density at the skin surface between 14 and 73µW/cm² and induces an electrical field of about 10 mV/cm, resulting in adsorbed power levels in the range of 7.3µW/cm3. This provides field exposure levels at the target tissue that are five to nine orders of magnitude above the thresholds which have been established for non-thermal electromagnetically induced biological effects at the cell and tissue level.

Results

A total of ninety-one (91) women were enrolled with moderately severe dysmenorrhea and were randomly assigned an active or control Allay Menstrual Pain Therapy device. Forty-eight (48) patients received active devices while the remaining forty-three (43) received placebo devices. The patients ranged in age from 18-34 years, with an average age of 26.2. Seventy-five percent (75%) of the subjects were White and fifteen percent (15%) of the subjects were Asian. A further breakdown is included below:

Patient Age Range: 18-34	Average Age
Indianapolis	28.6
San Francisco	24.9
Active Group	27.3
Placebo Group	27.8
	26.2

	IN	SF	Total
Active	23	25	48
Placebo	24	19	43
Total	47	44	91

Race	Qty	%
White	68	**74.73%**
Black	7	**7.69%**
Hispanic	2	**2.20%**
Asian	14	**15.38%**
	91	

Twenty-one (23.1%) subjects discontinued prematurely. However, 95% of subjects remained in the study for Days 1 and 2 (most severe days) of their menstrual cycles. Seven percent discontinued use due to wear issues (indicated below), and five percent discontinued use because their pain was eliminated. Although the data shows that ten percent of participants indicated that they discontinued use because the device didn't help their menstrual pain, this statistic includes the individuals given the placebo patch.
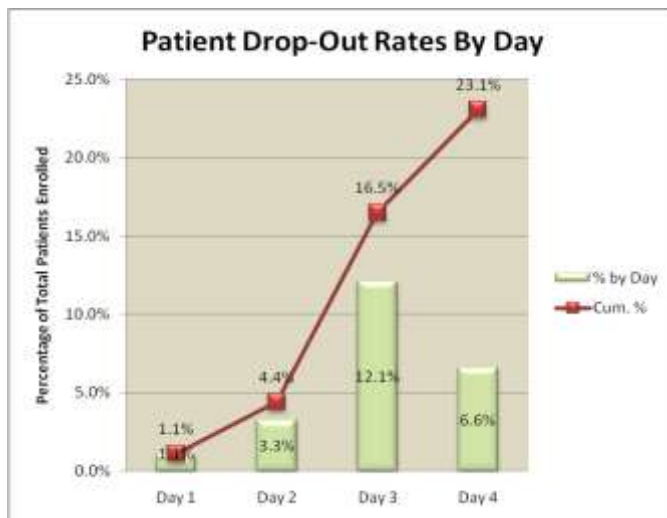
Drop-out Rates

	IN	SF	Total	% by Day	Cum. Drop-Outs	Cum. %
Day 1	1	0	1	1.1%	1	1.1%
Day 2	1	2	3	3.3%	4	4.4%
Day 3	5	6	11	12.1%	15	16.5%
Day 4	3	3	6	6.6%	21	23.1%

Patient Drop-Out Rates By Day

Reasons Indicated for Drop-Out

Pain Was Eliminated	4	4.4%
Adverse Events	0	0.0%
Wear Issues	7	7.7%
Device Didn't Help	9	9.9%
Lost Device	1	1.1%
Other	-	-

Device Wear Issues	Qty	% of Study Participants
Moistness	2	2.20%
Irritation	1	1.10%
Placement Stability	7	7.69%
BioElectronics Corporation **Total**	**10**	**10.99%**

Efficacy Results

This clinical study evaluating Allay Menstrual Pain Therapy showed that 77.1% of women using the active Allay patch reported either complete elimination or reduction in their typical menstrual pain and discomfort. Within this group, 17 (35.4%) reported least a 50% reduction in pain.

	Composite Pain Score				
	Estimated Percentage Pain Relief (Average)				
			# Patients		
	%	Active	Placebo	Active	Placebo
	0-10% (no change)	11	37	22.92%	86.05%
Positive Responders	10-25%	9		18.75%	
	25-50%	11	6	22.92%	13.95%
	50-75%	14		29.17%	
	75-100%	3		6.25%	
	Totals	48	43	100.00%	1

	Active	% of Active	Placebo	% of Placebo
Negative Responders	11	22.9%	37	86.0%
Positive Responders	37	77.1%	6	14.0%
Totals	48		43	
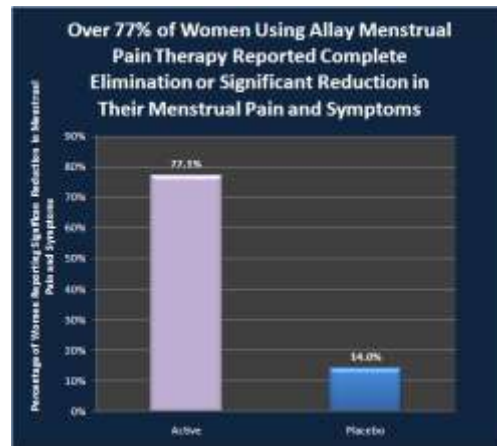
Relative to the active group, in the placebo (control) group, six studies (13.95%) reported a reduction in their menstrual pain symptoms. The differences in positive response to either the active or control device was of statistical significance ($p < 0.05$).

Although the actual levels of pain indicated are subjective and vary by patient, the change in pain levels is the leading factor in determining efficacy. On average, pain was decreased significantly on a daily basis, as indicated in the table and charts below. The clinical results also indicate that over time the percentage of decrease in pain increases, suggesting that there is a strong correlation between duration of use of Allay and pain reduction. By Day 5, pain had been reduced by 63.2%, compared to a reduction of 31.3% on Day 1.

	Control: Normal Daily Pain	Therapy: With Allay	% Decrease in Pain
Day 1	8.3	5.7	31.3%
Day 2	7.9	4.8	39.2%
Day 3	7.4	4.3	41.9%
Day 4	6.5	3.4	47.7%
Day 5	5.7	2.1	63.2%
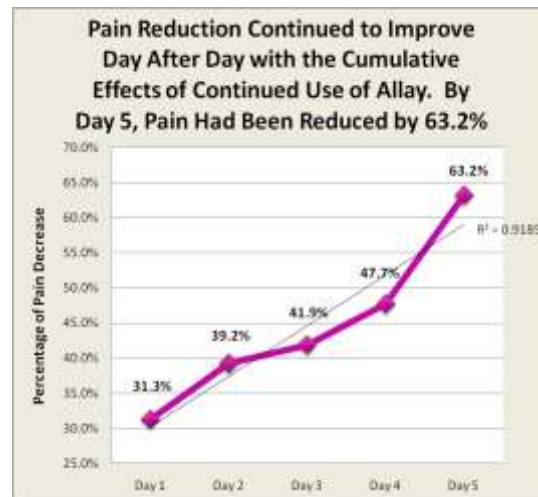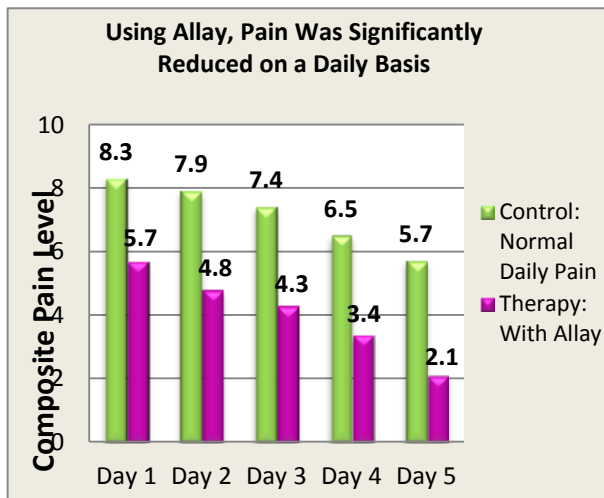
Although this correlation is also affected by the body's natural tendency to reduce pain over time, the pain levels were significantly lower with use of Allay, and the rate at which pain decreased was significantly higher at the onset and end of patients' menstrual cycles. For instance, from Day 1 to Day 2, pain decreased at a rate of 1.25x the body's perceived normal rate of pain reduction.

	Control: Normal Daily Pain	Diff	Therapy: With Allay	Diff	% Decrease in Pain	Rate Increase of Pain Reduction
Day 1	8.3		5.7		31.3%	
Day 2	7.9	0.4	4.8	0.9	39.2%	125.0%
Day 3	7.4	0.5	4.3	0.5	41.9%	0.0%
Day 4	6.5	0.9	3.4	0.9	47.7%	0.0%
Day 5	5.7	0.8	2.1	1.3	63.2%	62.5%
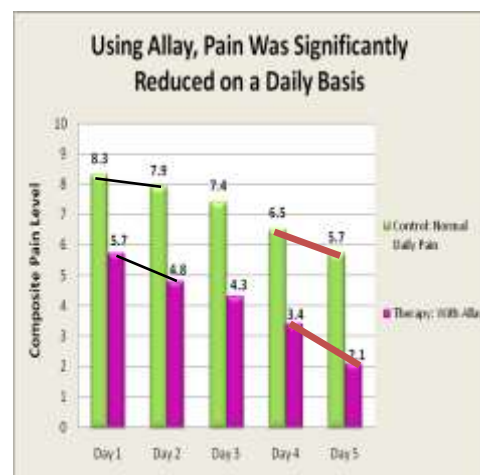
The overall slopes of -0.66 and -0.86 for normal and Allay pain decrease, respectively, also suggest that pain may be reduced at a slightly faster rate overall with use of Allay, although not statistically significant.

Safety Results

One subject discontinued early from slight irritation, but there was no evidence of a clinically significant effect. No (zero) subjects experienced adverse events.

Adverse Events	0

Outcome Measure Results

Satisfaction with treatment was qualitatively assessed by subject-reported patience adherence, treatment satisfaction, and symptoms questionnaire. Comments are included in Appendix A.

Conclusion

The clinical study demonstrates that the Allay Menstrual Pain Therapy is an effective and safe non-drug method for use in the treatment of primary dysmenorrhea. Allay can be offered as a primary, drug-free treatment method for women suffering from moderate dysmenorrhea. In more severe cases of dysmenorrhea, it can be an adjuvant treatment to reduce the duration of use or the amount of other oral medications.

Discussion

Menstrual cramps and pain are the result of contractions of the uterus. Prostaglandins stimulate the uterine muscles to contract and shed its lining. Women who have high levels of prostaglandins will experience more intense contractions of their uterus and subsequently more pain. The benefit of anti-inflammatory medications is directed towards modulating one's responsiveness to prostaglandin levels. Unfortunately, anti-inflammatory medications are not always completely effective at relieving menstrual pain and they have well-known side effects as well. A non-drug alternative would be a novel approach to the treatment of menstrual pain and would address a significant unmet need.

This clinical study has demonstrated that the Allay menstrual patch is effective at reducing and/or ameliorating the pain from dysmenorrhea. It is statistically significant that the active patch group exhibited a 77% positive response compared to just a 9% positive response in the placebo. It does so with no reported side effects other than some wear issues undoubtedly related to the design or material issues of the patch.

The exact mechanism by which the PEMF of the Allay patch works for menstrual pain is currently speculative. Certainly, the placebo enhancement effect plays a role but that alone cannot exclusively account for the study results, particularly in the face of such a discrepant and very low positive response to the control group patches. Modulation of pain pathways is one potential explanation Pain signals are transmitted along nerve cells to pre-synaptic terminals.

PEMF has been shown to result in pre-synaptic terminals that have slowed release of neurotransmitters by altering membrane potentials thus blocking or reducing pain signals. Another potential mechanism is the well-known anti-inflammatory PEMF by affecting T-cell activity and inflammatory mediator releases. It is likely that the cumulative effect of all of these three different mechanisms accounts for the positive responses seen.

PEMF therapy appears to have a role in the management of pain from dysmenorrhea which is currently dominated by pharmaceutical and some surgical treatments. PEMF offers a noninvasive approach with no side effects and no potential for drug interactions.

The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: A case report
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Ian M Rawe[1], Ph.D

Tracey C Vlahovic[2], DPM

1. Bioelectronics Corporation, Frederick , Maryland

2. Temple University School of Podiatric Medicine, Philadelphia, Pennsylvania, USA.

Contact and request for reprints:

Ian M Rawe Ph.D
BioElectronics Corp.
4539 Metropolitan Ct.
Frederick, MD 21704
781-325-2439
301-874-6935 Fax
Ian.rawe@gmail.com

Abstract

Introduction

Pulsed radio frequency energy (PRFE) has successfully been used to treat diabetic and venous stasis ulcers. In this case report, a lightweight wearable form of a PFRE device was evaluated and used to treat 3 diabetic foot ulcers and 1 venous stasis ulcer.

Methods

The ulcers were present on the 4 patients for greater than 3 months and had failed to heal after conventional treatment. A lightweight battery powered, wearable form PRFE device was introduced as a treatment and used 6-8 hrs per day for a period of 6 weeks.

Results

All patients after 1 week of therapy showed improvement and wound size was seen to decrease. Patient 1 had a venous stasis ulcer, and reported significant pain relief after 2 weeks treatment. Patients 2 and 3 achieved complete healing after 3 weeks treatment, and patient 1 and patient 4 had a 95% and 88% reduction in wound size after the 6 week study period. Both these patients continued to complete healing using the PRFE device after the 6 week study period.

Conclusion

PRFE treatment delivered in the form of a wearable lightweight patch appears to offer promise in the treatment of recalcitrant chronic wounds.

Keywords: chronic device healing PRFE wounds

Introduction

Diabetic foot ulcers are the most common chronic wounds in western industrialized countries. Of the millions who have diabetes mellitus, 15 per cent will suffer foot ulceration which often leads to amputation (100,000 per annum in the US alone). The economic burden of treating diabetes as its associated complications is extreme(1) and will likely increase as the rate of diabetes continues to rise. Statistics from the American Diabetes Association show the prevalence of diabetes at 25.8 million children and adults, or 8.3% of the US population. Venous stasis ulcers are a major cause of chronic wounds, and are typically associated with significant pain. Venous stasis ulcers are common in patients who have a history of leg swelling, varicose veins, or a history of blood clots in either the superficial or the deep veins of the legs. Venous ulcers is the most common etiology of lower extremity ulceration, affecting approximately 1 percent of the U.S. population (2).

The healing of diabetic foot ulcers, is necessary for the prevention of amputation and a number of advanced technologies have been introduced to achieve higher success in amputation prevention and limb preservation(3). Electrotherapy in the form of pulsed radio frequency electromagnetic energy (PRFE) has recently received a new focus, with a number of case reports showing promising results in the healing of chronic wounds (4-8). A retrospective study on the Regenesis Wound Healing Registry (Regenesis Biomedical, Scottsdale, Arizona) has indicated that PRFE therapy holds promise to be an effective treatment for chronic wounds(9). Regensis Biomedical's Provant System is a suitcase sized device that emits non-ionizing, radio frequency energy at 27.12 MHz There is a growing list of clinical studies that have shown the safety and efficacy of PRFE as a therapy, as has been recently reviewed by Guo et al, 2011(10). However, there are still major limitations to PRFE devices, as treatment regimens require 2 x 30 minute treatments per day, making it impractical for most ambulatory patients, restricting it's use to severe chronic wounds.

In this case report we show the application of a wearable battery powered form of PRFE device for the treatment of recalcitrant wounds. The lower energy levels emitted by this form of PRFE device are compensated by extended use times. The PRFE device used in this case study was ActiPatch™ (BioElectronics Corporation, Frederick, MD) which delivers PRFE at a carrier frequency of 27.12 MHz and a pulse rate of 1000Hz.

Materials and Methods

At the Temple University Foot and Ankle Institute, four adult African American diabetic males between the ages of 40 to 75 with ulcers present for longer than three months were admitted into the pilot study. Three patients had diabetic neuropathic ulcers and one had a venous stasis ulcer. All the diabetic ulcer patients had at least one palpable pedal pulse and an ulcer of Wagner Grade II or higher.

All ulcers had previously been treated with a variety of methods, without appreciable healing, and are described for each patient. **Patient 1:** was a 72yr with type II diabetes that had a venous stasis ulcer that had undergone multilayer compression therapy for 4 weeks without any appreciable healing. Significant pain was experienced by this patient which was assessed by a 0-10 point visual analogue scale (VAS). **Patient 2:** was 42 yrs old with type II diabetes and an

actively working truck driver. Previous failed treatment included wound debridement, use of Promogran matrix, and dry sterile dressing. Once the PRFE device was added to the regimen, Promogran was discontinued**. Patient 3:** 62 year old patient with insulin controlled diabetes that had not responded to debridement and application of triple antibiotic ointment with offloading. Once the PRFE device was added, triple antibiotic was discontinued. **Patient 4:** 74 year old patient with insulin controlled diabetes presented with a right heel decubitus heel ulcer that resulted following hospitalization for prostate surgery. Patient had already had a below knee amputation on the left side. The right heel wound was granular and non-infected. Offloading with a protective boot and wound care consisting of debridement, Promogran matrix, and dry sterile dressings were done prior to the PRFE device use. Once the PRFE device was used, weekly debridement and offloading was maintained.   After informed consent, patients adopted a protocol that utilized the PRFE device for six to eight hours per day. The patients with diabetic ulcers, had their wounds covered with moist saline gauze, ActiPatch™, and a dry sterile dressing. When the ActiPatch™ PRFE device was not in use, the ulcer was covered with moist saline gauze and dry sterile dressing. Compression therapy was continued with patient 1 along with the PRFE device for 6-8 hours per day. Patients kept a journal of their PFRE device use and brought the log in during their weekly visits. Weekly visits consisted of sharp debridement and surgical scrub, for the diabetic ulcer patients, followed by measurement and photographic documentation. Wounds were evaluated for any signs of infection and new changes such as increased depth or drainage. The PFRE device was also evaluated for proper functioning at each visit.   Patients were educated on their daily wound dressing changes. The wounds were evaluated once weekly for a total of six weeks.

Results

The patients tolerated the PRFE therapy well and reported no negative side effects. Wounds still needed to be sharply debrided on a weekly basis, but patients were pleased with the therapy and its ease of use at home. Table 1 shows the wound measurements at the start of the treatment (week 0) and for the following 6 weeks of treatment. Starting at week 1 all patients were seen to have a decrease in wound size. The ulcers had a steady decrease in side to side closure and in visible peri-wound edema. Patients 2 and patient 3 had complete healing of their diabetic ulcers after 3 weeks of treatment.

Patient 1 had a venous stasis ulcer show in Figure 1, which caused the patient significant pain. After two weeks of PRFE therapy the patient reported significant pain relief. The ulcer of patient 1 decreased in size from 4 x 2.5 cm to 0.7 x 0.5 cm at the end of the 6 week study period, a decrease of approximately 95% of the wound area. The venous stasis continued to complete healing after the study period with continued use of the PRFE therapy device.

Figure 1. The venous stasis ulcer of patient 1 is shown at week 0 , week 2, week, 4 and week 6 of PRFE treatment. Significant pain relief was reported by the patient after 2 weeks treatment. The ulcer had decreased in size from 4.0 x 2.5 cm to 0.7 x 0.5 cm after 6 weeks PRFE treatment. The ulcer continued onto healing using the PRFE therapy.

WEEK 0   WEEK 2

WEEK 4   WEEK 6

Figure 2 shows the left heal ulcer of patient 3. The ulcer improved rapidly with PRFE treatment, recovering 50% of the wound area after 1 week of PRFE treatment. The ulcer progressed to complete healing at 3 weeks. The ulcer is shown at week 0, week 1, week 2 and week 3.

WEEK 0WEEK 1   WEEK 2   WEEK 3

Table 1 Shows the wound size (centimeters) data of each patient at week 0 (start of treatment) and for each week of the 6 week study period.

Patient	Age	Location	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
1	66	right leg	4 x 2.5	4 x 2.3	4 x 2	3 x 1.5	2 x 1.5	1 x 0.7	0.7 x 0.5
2	60	right foot	0.5 x 0.5	0.3 x0.3	0.2 x 0.1	ulcer healed			
3	43	left heel	4 x 1	2 x 0.5	1 x 0.3	ulcer healed			
4	74	right heel	2.5 x 1.75	2 X 2	2 X 1.5	1.7 X 0.7	1 X 1	1 X 0.5	1 X 0.5

The diabetic ulcer of patient 4 had a wound size at the beginning of treatment of 2.5 x 1.75 cm, by week 4 this had decreased to 1 x 1 cm, approximately a 73% reduction in size and by week 6 the wound area decreased to 1 x 0.5 cm, a reduction of 88% in size. Wound area reduction at week 1 and week 4 is a strong indicator of complete healing(10). Patient d 4 had significant reduction in wound size at 6 weeks and continued on to healing after the study period utilizing the PRFE treatment.

Figure 3. Patient 2 had a 0.5 x 0.5 cm diabetic ulcer at the beginning of PFRE treatment, which healed after 3 weeks PRFE therapy. The ulcer at week 0, week 1 and week 3 is shown.

WEEK 0 WEEK 1 WEEK 3

Discussion

The mechanism by which PRFE promotes the healing of chronic wounds is not fully understood. But studies on cells and animals have given insight into the effects of PRFE therapy. Up-regulation of gene families involved in tissue repair in co-cultures of human dermal fibroblasts and epidermal keratinocytes treated with PRFE has been shown(Moffett, Griffin et al. 2010) . These included metalloproteinase and tissue inhibitor of metalloproteinase, and interleukin - related genes, interferon-related genes, and tumor necrosis factor-related genes. Cell studies have demonstrated up-regulation of FGF-2 after PRFE exposure, an important molecule in wound healing for promoting endothelial cell proliferation, angiogenesis and granulation tissue formation. PRFE therapy given to animal wound models of diabetes have reported to an up-regulation of FGF-2(12), increased wound healing, and wound tensile strength compared to sham control animals(13,14).

A portable wearable PRFE device was first used in 1982 for the treatment of postoperative wounds following blepharoplasty(15). A study by Stiller et al 1993, using a wearable form of PFRE device evaluated its clinical efficacy and safety in a placebo controlled multicenter trial. Significant decreases in wound depth and pain intensity favoring the active group were seen, wounds after 8 weeks treatment   in the active group had a 47.7% decrease in wound surface area vs. a 42.3% increase for placebo(16)(Stiller, Pak et al. 1992). The device used in this study weighed 505 grams and was used 3 hrs per day. More recently clinical trials on the postoperative recovery after breast augmentation surgery(Heden and Pilla 2008) , and breast reduction surgery(18) have clearly demonstrated the control of postoperative pain with newer versions of wearable, portable PRFE devices.

In this pilot study presented here, a light weight wearable form of PRFE was used to facilitate the wound healing process in both diabetic and venous stasis lower extremity ulcers. The PRFE device used in this case study was a in the form a patch and was easy to use from both the physician's and patient's standpoint. Since the completion of this study ActiPatch has been refined and updated, and now consists of a small control module and a 12 cm, or 8 cm antenna and weighs approximately 8 grams. The reconfigured device is now used as a 24 hr continuous PRFE therapy with the same carrier frequency of 27.12 MHz and 1000Hz pulse rate. Figure 4 shows the application of the PRFE device on a patient with a venous stasis ulcer, prior to PRFE therapy this patient was considered for amputation, however, the ulcer healed within 8 weeks and the patient avoided amputation (unpublished data).

The results from this pilot study suggest that lightweight wearable PRFE devices maybe an effective adjunct therapy for recalcitrant wounds promoting healing and reducing pain. The ease of use, low cost and compatibility with current conventional therapy also suggest this form of wearable PRFE device could be widely applied as a first choice therapy, though further studies are required to determine their true value.

Figure 4. A version of PRFE device is shown in use on a patient with a venous stasis ulcer

References

1.   Driver VR, Fabbi,M, Lavery LA, Gibbons G. The costs of diabetic foot: the economic case for the limb salvage team. J Am Podiatr Med Assoc 2010;100(5): 335-341.
2.   Collins L, Seraj, S. Diagnosis and treatment of venous ulcers. Am Fam Physicians 2010;81(8):989-96.
3.   Wu SC, Marston W, Armstrong DG. Wound care: the role of advanced wound healing technologies. J Vasc Surg 52(3 Suppl) 2010;59S-66S.
4.   Larsen JA, Overstreet J.Pulsed radio frequency energy in the treatment of complex diabetic foot wounds: two cases. J Wound Ostomy Continence Nurs 2008;35(5): 523-527.
5.   Porreca EG, Giordano-Jablon GM. Treatment of severe (Stage III and IV) chronic pressure ulcers using pulsed radio frequency energy in a quadriplegic patient. Eplasty 2008;8: e49.
6.   Fletcher S. Successful treatment of venous stasis ulcers with combination compression therapy and pulsed radio frequency energy in a patient scheduled for amputation. J Wound Ostomy Continence Nurs 2011;38(1): 91-94.
7.   Frykberg R, Martin E, Tallis A, Tierney E. A case history of multimodal therapy in healing a complicated diabetic foot wound: negative pressure, dermal replacement and pulsed radio frequency energy therapies, Int Wound J 2011;8, 132-139.
8.   Maier M. Pulsed radio frequency energy in the treatment of painful chronic cutaneous wounds: a report of two cases. Pain Med 2011;12(5): 829-832.
9.   Frykberg RG, Driver VR, Lavery LA, Armstrong DG, Isenberg RA. The Use of Pulsed Radio Frequency Energy Therapy in Treating Lower Extremity Wounds: Results of a Retrospective Study of a Wound Registry. Ostomy Wound Manage 2011;57(3): 22-29.
10.   Guo L, Kubat NJ, Isenberg RA. Pulsed radio frequency energy (PRFE) use in human medical applications. Electromagn Biol Med 2011;30(1): 21-45.
11.   Lavery LA, Barnes SA, Keith MS, Seaman JW Jr, Armstrong DG. Prediction of healing for postoperative diabetic foot wounds based on early wound area progression. Diabetes Care 2008;31(1): 26-29.
12.   Moffett J., Griffin N, Ritz M, George F. Pulsed radio frequency energy field treatment of cells in culture results in increased expression of genes involved in the inflammation phase of lower extremity diabetic wound healing, The Journal of Diabetic Foot Complications 2010;2, 57-64.
13.   Callaghan MJ, Chang EI, Seiser N, Aarabi, S, Ghali, S, Kinnucan, ER, Simon BJ, and Gurtner GC. Pulsed electromagnetic fields accelerate normal and diabetic wound healing by increasing endogenous FGF-2 release, Plast Reconstr Surg 2008;121, 130-141.
14.   Goudarzi I, Hajizadeh S, Salmani, ME, Abrari, K. Pulsed electromagnetic fields accelerate wound healing in the skin of diabetic rats, Bioelectromagnetics 2010;31, 318-323.
15.   Li Q, Kao H, Matros E, Peng C, Murphy GF, Guo L. Pulsed Radio Frequency Energy (PRFE) Accelerates Wound Healing In Diabetic Mice. Plast Reconstr Surg 2011; Feb 8

16.   Nicolle FV, Bentall RM.. Use of radio-frequency pulsed energy in the control of postoperative eaction in blepharoplasty. Aesthetic Plast Surg 1982;6(3): 169-171.

17.   Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992;127(2): 147-154.

18.   Heden P, Pilla AA. Effects of pulsed electromagnetic fields on postoperative pain: a double-blind randomized pilot study in breast augmentation patients. Aesthetic Plast Surg 2008l;32(4): 660-666.

19.   Rohde C, Chiang A, Adipoju O, Casper D, Pilla AA. (2010) Effects of pulsed electromagnetic fields on interleukin-1 beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients, Plast Reconstr Surg 125, 1620-1629.

Physician Conducted Pilots and Testimonials.

ActiPatch and Rapid Recovery Breast Augmentation Study (Dr. Barry Eppley, M.D.)

Contemporary recovery after breast augmentation is designed to be short with minimal disruption of one's lifestyle. Anti-inflammatory medications and early physical therapy of the arms (the attachments of the pectorals muscle) are the mainstays of an aggressive recovery program after the placement of breast implants. Gone are the need for bulky dressings and restrictions on physical activity after surgery which had been the hallmarks of breast implant surgery in the past. The less pain a patient has, the more physical therapy they can do to further expedite their return to normal activities of daily living. In an effort to control pain after breast augmentation, I often employ pulsed electromagnetic therapy using ActiPatch topical patches devices. To determine whether this was actually beneficial or just a psychotherapeutic concept, a prospective clinical study of breast augmentation patients was done.

A prospective clinical study of fourty-eight (48) women undergoing breast augmentation was conducted from November 2007 to November 2008. Women underwent breast augmentation with either saline or silicone breast implants through a transaxillary (saline) or inframammary (silicone) incision. Patients were aware that they would receive ActiPatch therapy as part of their postoperative protocol. At the completion of surgery, ActiPatch devices (crescent-shaped) were placed over the medial and superior aspect of the breasts (over the pectorals muscle) and taped into position inside their surgical bra. For the first twenty patients, the device was activated (activating tab pulled) on the left breast and on the opposite right breast the device was not activated. (activating tab was trimmed but not pulled) The patients were not informed which devices were which. In the next twenty-eight patients, the device locations were reversed. Patients were instructed to wear the devices for the first seventy-two hours after surgery after which they were to be discarded. Patients were given a sheet to complete at the time of discontinuing their ActiPatch therapy so that they could rate their postoperative pain on a simple

scale (1 - 10) and, most importantly, compare and rate the pain between the two breasts at that time period.

In the first twenty patients, fourteen rated the active device breast as less uncomfortable than the control patch side. In the next twenty-eight patients, twenty-one rated the active side less painful. In total, thirty-five patients (73%) reported less pain and more comfort ability on the breast that received pulsed electromagnetic therapy than on the control side.

Pulsed electromagnetic therapy has been around for a long time and its potential benefits are based on creating an anti-inflammatory effect. ActiPatch provides a simple, low-cost method of delivery of this potential healing technology. In this breast augmentation study, ActiPatch demonstrated less pain within the first few days after surgery. Given its ease of use and lack of any potential for creating any adverse problems, its use as part of a breast augmentation recovery protocol appears to have offer patients some real benefits.

While all pain studies are flawed, and this one is no exception, it certainly suggests that pulsed electromagnetic therapy (PEMT) should be further explored. A change in the design of the device so that it 'fits' the breast better may be even more useful. A large round loop that would fit around the circumference of the breast is more likely to deliver the effects of PEMT to the breast in a more even distribution although I could argue that the pain after breast augmentation is muscular rather than 'breast' in origin.

ACTIPATCH - A New way of treatment, Pilot investigation of 52 patients in general praxsis.

Evaluated September – October 2008

Jørn Bennedbæk, MD

Hypothesis of treatment

In living healthy cells the potential of the membrane potential is stable equals rest potential. The inside of the membrane is negative in relation to the outside. Most of our cells have a rest potential in the membrane in the range about 70 mill volt. When it increases it is hyperpolarized , if it decreases the membrane will depolarise. If the 70 millivolt is valued as a field over the 7 nanometer thick membrane, the strength of the field equals 10.000 volt pr.mm. Changes in the environment/field has direct effect on conformation of proteins in the plasma membrane and due to this abilities of the composition of multi formations of amino acid (ref. 1) The synthesis of proteins in fibroblasts in electromagnetic fields has been investigated earlier (ref.2)

ActiPatch uses the modulated radio frequencies generated electromagnetic field to induce the low-frequent membrane stabilizing pulse, with amplitude in the field of 1 kHz / 100 uV/cm the membrane will due to this, be forced to re-establish the rest potential.

The effect can be at more points. Stabilizing the cell. Improvement of Cell-to-cell communication. Improvement of the neuron-transmission. The direct and indirect effect in inhibition of the inflammation process at all levels.

Duration of treatment

The patients received instructions in use with application from bedtime until morning every day for one week. The effect had to be noted on a visual scale from 0-5, where (vs5) is maximal (start) pain and (vs0) no-¨pain. Duration of the test was 7 days.

Diagnosis and results

3 patients with fascitis pedis. 1 pain free after 5 days, 1 after 6 days No..3 was on stage (vs1) after 7 days.

7 patients with epicondylitis lateralis. 1 was free of pain day 4, 4 on day 6, and 1 had only slight pain (vs2) on day 7. 1 * had no effect.

2 patients with epicondylitis medialis had no pain, whatsoever on day 6.

4 patients with tibialis anterior syndrome. 2 were free of pain after 3 days and 2 on day 5 .

2 patients with Mb.Osgood-Schlatter had no effect after 7 days.

2 patients with pes anserinus tendinitis had only slight problems on day 7 dage (vs1)

3 patients with polyartrosis manuum verified also as arthritis rheumatoides . 2 had no pain after 6 days, 1 had only slight problems on day 7 (vs2)

2 patients with arthritis urica. On day 7 one had only slight pain (vs1) and the other had moderate pain (vs3)

8 patients with myosis lumbale et paravertebrale without referred pain or neurological deficits. 3 had no pain on day 4 ,2 on day 5 . 1 on day 6. and 2 had only slight problems on day 7 (vs2)

2 patients with pain one year after surgery for cervical prolaps of discus. No effect.

2 patients with pain one year after surgery for lumbal prolaps of discus .1 had moderate pain day 7 (vs2) 1 had no effect.

3 with distorsio pedis/laesio lig. talofibulare anterior. 2 had no pain day 6. 1 had day 7 only slight problems (vs1)

8 patients with various tendinites of wrest /forehand and antebrachium (flexors and brachioradialis). 4 had no pain day 3. 1 on day 4 1 on day 5 and 1 on day 6.dag. 1 had no effect .

4 patients with tendinitis of Achilles. 3 had no pain day 5 .1 on day 6.

* Had earlier operation on pronator teres syndrome bilateralis.

Discussion

AP has proved convincing effect at many conditions. There were neither side-effects reported nor complaints of any kind. The device is simple and easy to handle.

Spontaneous remission would appear at more of the patients in this investigation, but how fast in relation to these results?

2 patients with rheumatoid arthritis concluded the relief of pain just as effective as the treatment of steroids in high-dose for short periods, but faster effect.

In this pilot project, application was only 8 hours per day. The device may and can be used 24 hours per day. Could more of the patients have effect faster or some at least have had an effect if the device were used   permanently.   AP has power for 720 hours. The primary impression in effect of the treatment of patients with the diagnosis, where positive response has been notified is effect at least as effective as usually treatment, but with far faster onset of relief. AP has cell restitution effect and more test has been started in examination of wound healing and effect on post-operations conditions (healing process, haematoma etc.) and latest in treatment of psoriasis.

ActiPatch has been in use on more patients with ulcers of the lower limbs treated by nurses in the county.

Furthermore the joint pains of one psoriasis patient disappeared after 1 week of treatment. When stopped the joint pain came back after few days. Disappeared again with re-use of the AP for few days

More injuries from sport has been treated with AP and has proved excellent results. Many questions now and in the future will be asked in order to examine further possibilities and effects of the AP. Further investigation on a scientific basis has to be done to find right indications of treatment and duration of the many diseases potentially involved.

References

1.Suhr-Jessen, Peter (2004) Basis bog i Cellebiologi

2.McLeod,K.J., Lee,R.C., and Ehrlich, H.P.(1987) Frequency dependence of electric field modulation of protein synthesis in fibroblasts. Science 236: 1465-1469

ActiPatch Therapy Following Cosmetic Surgery of the Face and Neck: A Valuable Adjunct to the Postoperative Management

Casas, Laurie A., MD FACS

ActiPatch Therapy has become an integral part of the postoperative treatment plan/regime in my patients following Blepharoplasty, Rhinoplasty, Facelift, Neck lift and Liposuction of the Neck. After completing a Prospective Observational Study which evaluated the effects of using ActiPatch on 32 patients (52 procedures) as compared to a control group of 30 patients (45 procedures) who underwent the same cosmetic procedures without the use of ActiPatch, we found that ActiPatch Therapy decreased postoperative swelling, bruising , localized fibrosis and localized discomfort by 30-50%. Because of this Observational Study I have added ActiPatch Therapy to my postoperative protocol for patients undergoing cosmetic surgical procedures of the face and neck and who desire a decrease in their postoperative recovery time.

I performed a prospective observational study on 32 patients (52 procedures) using ActiPatch Therapy and compared them to 30 patients (45 procedures) control group to evaluate the effect of ActiPatch on postoperative 1) swelling and bruising, 2) localized subcutaneous fibrosis and 3) localized discomfort. Both groups of patients were on the same preoperative protocol of vitamin supplements and postoperative protocol which continued the use of supplements and added the use of Cox 2 inhibitors for localized pain. In addition, all patients had Manual Lymphatic Drainage with a specific protocol of 2 visits per week for 6 weeks. Both groups of patients were evaluated by a Nurse Practitioner, the treating physical therapist and the senior author at 3 days, 5-6 days, 7-10 days, 13-14 days, 21 days, 28 days and 42 days postoperatively. An observational data sheet was completed at each visit which documented 1) localized pain, 2) swelling and bruising, 3) the soft tissue fibrosis which is characterized by subcutaneous lumps and tightness and discomfort when moving the operated part. The ActiPatch was either placed under the gauze head wrap dressing in the facelift, neck lift and neck liposuction patients, and at the glabella or corner of the brow in the Rhinoplasty and Blepharoplasty patients. All patients used the ActiPatch for the first three days and some continued to use it for a total of ten days. The endpoint was when all visible bruising had resolved.

We found that ActiPatch therapy was very effective in decreasing postoperative swelling and bruising. Specifically, our observers noted a 30-50% reduction in the number of days the patients had visible swelling and ecchymosis compared to the control group. Both groups had Manual Lymphatic drainage and Deep Tissue Release Therapy scheduled for 2 times per week for six weeks.(ref: "Manual Lyphatic Drainage: An Integral Component of Postoperative Care in the Plastic Surgery Patient" Presented at the Annual Conference of the American Society of Lymphology, Chicago, IL August 1999 and "The role of Manual Lymphatic Drainage in the Postoperative Care of Cosmetic Plastic Surgery Patients", Presented at the Annual Conference of the American Society of Lymphology, Las Vegas, Nevada October,2004.) The ActiPatch group required 30-50% fewer sessions to decrease swelling, bruising and localized discomfort

from soft tissue fibrosis. The endpoint of Lymphatic Drainage Therapy is decided by both the patient and the therapist who together decide that the operated tissues feel and look normal.

ActiPatch Therapy is very useful to decrease the swelling, bruising and localized discomfort in patients undergoing cosmetic of the face and neck. The following protocol is now used in my practice for all patients who desire a decrease in their postoperative recovery time following Cosmetic Surgery of the face and neck.

Blepharoplasty: ActiPatch 500 either over each eyebrow, or at the corner of each brow or under each lower eyelid. 24 hours per day for 3-7 days. It is removed for showering and replaced by moistening the hydrogel. Some patients used paper tape to help hold the ActiPatch in position.

Rhinoplasty: ActiPatch 500 at the Glabella 24 hours per day for 3-7 days.

Facelift: ActiPatch 500 is placed on each preauricular area under the gauze head wrap dressing. When the dressing is removed the ActiPatch is placed either in the pre or post auricular area as the swelling drops down the face to the neck lymph nodes over the first 3-10 days after surgery.

Neck Lift: ActiPatch 500 is placed on both sides of the neck under the ear and under the gauze head wrap dressing. When the dressing is removed the ActiPatch is worn on the neck are where the most swelling and bruising is visible for the first 3-10 days.

Neck Liposuction: same protocol as Neck Lift.

ActiPatch is removed for showering and replaced by moistening the hyrogel. Some patients use paper tape to help hold the ActiPatch in position.

Abdominoplasty Post-Operative Pain Control with ActiPatch

Kimberley B.C. Goh, M.D.

An abdominoplasty is one of the most painful cosmetic body contouring procedures we perform. Fear of post-operative pain has always been an obstacle for patients when considering an abdominoplasty. There is now a new, portable, lightweight and low cost way to decrease postoperative pain. The ActiPatch is a device which produces pulsed electromagnetic therapy that helps reduce swelling, relieve pain and enhance healing.*

I have been using the ActiPatch 500 for postoperative abdominoplasties for about six months and have been very impressed at its pain control. Prior to ActiPatch I had been using oxycodone and diazepam for postoperative pain control with intra-operative marcaine placed under the flap prior to emergence from anesthesia. The patients complained of significant pain and usually needed additional prescriptions for both pain and muscle relaxers within four days of surgery and often again at one week. Since using ActiPatch postoperatively I have not written a supplemental prescription for pain control and they have some left over. Their narcotic and medication needs have now decreased approximately seventy five percent.

Initially four patients were placed on ActiPatch for pain control after abdominoplasties. All patients had standard abdominoplasties with muscle and skin tightening; one had an augment performed as well. The charts were reviewed and interviews performed retrospectively to the physician to evaluate postoperative pain and narcotic use.

The first patient, A., was a 44 year old woman who had three full term pregnancies and several months of nursing. She complained of loss of breast fullness and a saggy abdomen. Physical exam revealed ptosis and pseudoptosis of her breasts and a lax abdominal wall, especially the upper abdomen, and loose skin on the upper and lower abdomen. She underwent a standard abdominoplasty and a bilateral subglandular breast augment. The breast augment was performed using a smooth round saline Mentor implant 350cc filled to 400cc in subglandular position through an inframammary incision. The abdominoplasty resected about 40 X 13 centimeters of skin, and the diastasis recti was corrected (about an eight centimeter plication). Fourteen cc of ¼% marcaine was placed under the flap at closure. As the patient was emerging from anesthesia the ActiPatch 500 was placed on the epigastrum and attached using its adhesive pad directly on the skin.

In recovery she needed one oxycodone for immediate postoperative pain. The evening of surgery she rested comfortably, and on her first visit on postoperative day one she came for her appointment wearing makeup with her hair styled and had minimal complaints of pain. She had been taking only one oxycodone every six hours because she was afraid that it would hurt, but had no complaints of abdominal pain. She had her oxycodone changed to mepergan because of nausea, but used very little her first week. She said she felt "she could have run a marathon" and could not believe how little pain she had.

Patient B was a 30 year old woman with two full term pregnancies who complained of a lax abdomen after multiple pregnancies and a previous cesarean section five years prior. She

underwent a standard abdominoplasty. Of note is that she had undergone a scheduled knee surgery two days prior to her abdominoplasty in order to make her recovery simultaneous. At surgery she had a 14 X 46 centimeter skin resection and an eight centimeter tightening of her diastasis recti. Fifteen cc of ¼% marcaine was placed under the flap at closure. The ActiPatch 500 was activated and placed directly on the epigastrum after the wound was closed. In recovery she had one oxycodone given orally. The first evening postop she used less than one oxycodone and one diazepam every six hours. The first day postop she complained only of knee pain, and felt that the abdominoplasty was less painful than her previous cesarean section. She also came in wearing facial cosmetics and had her hair styled on her first day after surgery. Her first week post op she also used less than 20 each of diazepam and oxycodone.

Patient C was a33 year old nulliparous woman with a previous submuscular augment mastopexy who complained of inability to tighten her lower abdomen with diet and exercise. She underwent a standard abdominoplasty with resection of approximately 13 centimeter by 43 centimeter skin ellipse, and an eight centimeter diastasis recti plication. Postoperatively she had an ActiPatch 500 activated and applied to her epigastrum. In the recovery room she had one oxycodone orally for pain. The evening of surgery she took one and one 5 mg diazepam. By the evening of surgery her only pain was on moving to stand or recline. At rest she was pain free and reported less pain than her previous augment mastopexy. The following week she took one or two oxycodone a day.

Patient D was a 56 year old with one full term pregnancy who was interested in improving her saggy lower abdomen. She had a previous lower midline incision for a cesarean section and a right lower quadrant incision for a bone graft donor site. She had significant diastasis recti and a small abdominal pannus.   She underwent a standard abdominoplasty with repair of diastasis and right lower quadrant plication for asymmetrical laxity. She had a 15 X 42.5 skin resection and a six centimeter plication. She had 12 cc of ¼% marcaine placed prior to emergence under the flap. Postoperatively she had one ActiPatch 500 device placed on the epigastrum. In the recovery room she had one oxycodone, and the first evening of surgery, one diazepam and one oxycodone. The next few days she was taking one to two diazepam once a day and one oxycodone four times a day.   By the end of her first week she had taken about twenty of the oxycodone and even less of the diazepam.

The amount of pain relief with the ActiPatch after a major surgery is impressive. This retrospective review of patients' charts and interviews demonstrates a marked decrease in postoperative pain and use of narcotics in abdominoplasty. While the ActiPatch can assist with healing and reduce swelling, those benefits are difficult to appreciate in actual clinical practice. The amount of pain relief however is easier to evaluate. There is a marked decrease in the use of pain medications and as well as a significant increase in comfort level. It is currently a low cost, small, portable, narcotic free pain control device, and should be considered in all major abdominal surgeries.

Appendix

A table of publications which have used PRFE therapy at 27.12MHz to treat medical conditions:

Date	Injury - pain	Publication
1971	Oral surgery	Aronofsky, D. H. (1971). Reduction of dental postsurgical symptoms using nonthermal pulsed high-peakpower electromagnetic energy. Oral Surg. Oral Med. Oral Pathol. 32:688–696.
1978	Oral surgery	Hutchinson, D., Witt, S., Fairpo, C. G. (1978). Pulsed electromagnetic energy therapy in third molar surgery. Oral Surg. Oral Med. Oral Pathol. 46:748–754.
1981	Oral surgery	Rhodes, L. C. (1981). The adjective utilization of Diapulse therapy (pulse high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. Quart. NDA 39:166–175.
1968	Foot surgery	Kaplan, E. G., Weinstock, R. E. (1968). Clinical evaluation of diapulse as adjunctive therapy following foot surgery. J. Amer. Podiat. Assoc. 58:218–221.
1985	Foot surgery	Santiesteban, A. J., Grant, C. (1985). Post-surgical effect of pulsed shortwave therapy. J. Amer. Podiatr. Med.Assoc. 75:306–309.
1982	Breast augmentation surgery	Silver, H. (1982). Reduction of capsular contracture with two-stage augmentation mammaplasty and pulsed electromagnetic energy (Diapulse therapy). Plast. Reconstr. Surg. 69(5):802–808.
2008	Breast augmentation surgery	Heden, P., Pilla, A. A. (2008). Effects of pulsed electromagnetic fields on postoperative pain: a double-blindrandomized pilot study in breast augmentation patients. Aesthetic Plast. Surg. 32:660–666.
2010	Breast reduction surgery	Rohde, C., Chiang, A., Adipoju, O., et al. (2010). Effects of pulsed electromagnetic fields on interleukin-1beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients. PRS 125:1620–1627.
2002	Mastectomy surgery	Mayrovitz, H. N., Sims, N., Macdonaki, J. (2002). Effects of pulsed radio frequency diathermy on postmastectomy arm lymphedema and skin blood flow: a pilot investigation. Lymphology 35:353–356.
1982	Blepharoplasty surgery	Nicolle, F. V., Bentall, R. M. (1982). Use of radio-frequency pulsed energy in the control of postoperative reaction in blepharoplasty. Aesthetic Plast. Surg. 6:169–171.
1975	Orchidopexy	Bentall, R. H. C., Eckstein, H. B. (1975). A trial involving the use of pulsed electro-magnetic therapy on children undergoing orchidopexy. Zeitschrift fu¨r Kinderchirurgie 17(4):380–389.
1983	Hand injury	Barclay, V., Collier, R. J., Jones, A. (1983). Treatment of various hand injuries by pulsed electromagnetic energy (Diapulse). Physiotherapy 69:186–188.
1974	Acute ankle inversion	Wilson, D. H. (1974). Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. Physiotherapy 60:309–310.
1993	Grade I-II ankle sprains	Pennington, G. M., Danley, D. L., Sumko, M. H., et al. (1993). Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. Mil. Med. 158:101–104.
1978	Ankle and foot injury	Pasila, M., Visuri, T., Sundholm, A. (1978). Pulsating shortwave diathermy: value in treatment of recent ankle and foot sprains. Arch. Phys. Med. Rehab. 59:383–386.
2002	Heel pain	Shandles, I. D. P., J., Reynolds, K. L. (2002). Heel Neurooma: the egigma of recalcitrant heel pain and an innovative approach highlighting sixty surgical cases and areview of two hundred and fifty seven symptomatic but non-surgical cases. Foot 12:10–20.
1985	Lateral ankle sprain	Barker, A. T., et al. (1985). A double-blind clinical trial of low power shortwave therapy in the treatment of soft tissue injury. Physiotherapy 71:500–504.
2003	Acute calcaneal fracture	Buzzard, B. M., Pratt, R. K., Briggs, P. J., et al. (2003). Is pulsed shortwave diathermy better than ice therapy for the reduction of oedema following calcaneal fractures?: Preliminary trial. Physiotherapy 89: 734–742.
1990	Long-term neck pain	Foley-Nolan, D., Barry, C., Coughlan, R. J., et al. (1990). Pulsed high frequency (27 MHz) electromagnetic therapy for persistent neck pain. A double blind, placebo-controlled study of 20 patients. Orthopedics 13:445–451.

1992	Acute whiplash injury	Foley-Nolan, D., Moore, K., Codd, M., et al. (1992). Low energy high frequency pulsed electromagnetic therapy for acute whiplash injuries. A double blind randomized controlled study. Scand J Rehabil Med 24:51–59.
2006	Osteoarthritis (knee)	Jan, M. H., Chai, H. M., Wang, C. L., et al. (2006). Effects of repetitive shortwave diathermy for reducing synovitis in patients with knee osteoarthritis: an ultrasonographic study. Phys. Ther. 86: 236–244.
2005	Osteoarthritis (knee)	Laufer, Y., Zilberman, R., Porat, R., et al. (2005). Effect of pulsed short-wave diathermy on pain and function of subjects with osteoarthritis of the knee: a placebo-controlled double-blind clinical trial. Clin. Rehab. 19:255–263.
2005	Osteoarthritis (knee)	Callaghan, M. J., Whittaker, P. E., Grimes, S., et al. (2005). An evaluation of pulsed shortwave on knee osteoarthritis using radioleucoscintigraphy: a randomized, double blind, controlled trial. Joint Bone Spine 72:150–155.
1988	Osteoarthritis (weight bearing joint)	Svarcova, J., Trnavsky, K., Zvarova, J. (1988). The influence of ultrasound, galvanic currents and shortwave diathermy on pain intensity in patients with osteoarthritis. Scand. J. Rheumatol. 67:83–85.
1964	orthopedic	Cameron, B. M. (1964). A three phase evaluation of pulsed, high frequency, radio short waves (Diapulse): 646 patients. Amer. J. Orthop. 6:72–78.
1991	posttraumatic algoneurodystrophies	Comorosan, S., Pana, I., Pop, L., et al. (1991). The influence of pulsed high peak power electromagnetic energy (Diapulse) treatment on posttraumatic algoneurodystrophies. Rev. Roum. Physiol. 28:77–81.
1989	Perineal trauma post child birth	Grant, A., Sleep, J., McIntosh, J., et al. (1989). Ultrasound and pulsed electromagnetic energy treatment for perineal trauma. A randomized placebo-controlled trial. Br. J. Obstet. Gynaecol. 96:434–439.
1964	Surgical wound healing	Cameron, B. M. (1964). A three phase evaluation of pulsed, high frequency, radio short waves (Diapulse): 646 patients. Amer. J. Orthop. 6:72–78.
1981	Skin grafts	Goldin, J. H., Broadbent, N. R., Nancarrow, J. D., et al. (1981). The effects of Diapulse on the healing of wounds: a double-blind randomized controlled trial in man. Br. J. Plast. Surg. 34:267–270.
1995	Pressure ulcers	Salzberg, C. A., Cooper-Vastola, S. A., Perez, F. J., et al. (1995). The effects of non-thermal pulsed electromagnetic energy (Diapulse) on wound healing of pressure ulcers in spinal cord-injured patients: a randomized double-blind study. Wounds 7(1):11–16.
1999	Pressure ulcers	Kloth, L. C., Berman, J. E., Sutton, C. H., et al. (1999). Effect of pulsed radio frequency stimulation on wound healing: a double-blind pilot study. In: Bersani, F. Electricity and Magnetism in Biology and Medicine (pp. 875–878). New York: Academic/Plenum.
1996	Pressure ulcers	Seaborne, D., Quirion-DeGirardi, C., Rousseau, M., et al. (1996). The treatment of pressure sores using pulsed electromagnetic energy (PEME). Physiother. Cancer 48:131–137.
1991	Stage II-III pressure ulcers	Itoh, M., Montemayor, Jr, J. S., Matsumoto, E., et al. (1991). Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 4:24–25, 29–34.
1995	Stage II,III and IV decubitus ulcers	Tung, S., Khaski, A., Milano, E., et al. (1995). The application of diapulse in the treatment of decubitus ulcers: case reports. Contemp. Surg. 47:27–33.
2008	Complex diabetic foo wounds	Larsen, J. A., Overstreet, J. (2008). Pulsed radio frequency energy in the treatment of complex diabetic foot wounds. J. WOCN 35(5): 523–527.
2008	Stage III and IV pressure ulcers	Porreca, E. G., Giordano-Jablon, G. M. (2008). Treatment of severe (stage III and IV) chronic pressure ulcers using pulsed radio frequency energy in a quadriplegic patient. Eplasty 8:e49.
2009	Chronic wounds	Frykberg, R., Tierney, E., Tallis, A., et al. (2009). Cell proliferation induction: healing chronic wounds through low-energy pulsed radiofrequency. Int. J. Low Extrem. Wounds 8:45–51.
2011	Venous stasis ulcers	Fletcher, S. (2011). Successful treatment of venous stasis ulcers with combination compression therapy and pulsed radio frequency energy in a patient scheduled for amputation. J Wound Ostomy Continence Nurs *38*, 91-94.
2011	Chronic wounds	Rawe, I.M., and Vlahovic, T.C. (2011). The use of a portable, wearable form of pulsed radio frequency electromagnetic energy device for the healing of recalcitrant ulcers: A case report. Int Wound J.
2010	Chronic wound registry	Frykberg, R.G., Driver, V.R., Lavery, L.A., Armstrong, D.G., and Isenberg, R.A. (2011). The Use of Pulsed Radio Frequency Energy Therapy in Treating Lower Extremity Wounds: Results of a Retrospective Study of a Wound Registry. Ostomy Wound Manage *57*, 22-29.
2011	Chronic cutaneous wounds	Maier M. Pulsed radio frequency energy in the treatment of painful chronic cutaneous wounds: a report of two cases. Pain Med. 2011 May;12(5):829-32

Market Clearances of BioElectronics Product Range

Country	Allay™	ActiPatch®	RecoveryRx™
All European Union Countries	✓	✓	✓
Korea		✓	
Italy	✓	✓	✓
Canada	✓	✓	✓
Nigeria	✓	✓	✓
Iran	✓	✓	✓
Jordan	✓	✓	✓
Kuwait	✓	✓	✓
Columbia	✓	✓	✓
Peru	✓	✓	✓
New Zealand	✓	✓	✓
Australia	✓	✓	✓
United States			✓

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